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REMARKS AT THE PRESENTATION OF THE CANDIDATES FOR THE DEGREE OF DOCTOR OF MEDICINE AT THE COMMENCEMENT OF THE JOHNS HOPKINS UNIVERSITY, JUNE 14, 1898.

By William H. Welch, M. D., *Dean of the Medical Faculty.*

Mr. President, Gentlemen of the Board of Trustees, Ladies and Gentlemen:

As this is only the second class to receive the degree of Doctor of Medicine from this University, it will not be inappropriate, before presenting the candidates for the degree, to say a few words concerning the development and aims of the recently organized Medical Department of the University.

Through the munificent gift of Miss Mary Elizabeth Garrett, added to a smaller but generous contribution from other public-spirited women, and supplementing the available resources of the University and Hospital, the Trustees of the University were enabled to open the Medical Department for the instruction of men and women on the second of October, 1893. At two previous commencement exercises the opportunity has been afforded me to present in some detail the plan of organization and the purposes of the new Medical School, and it is not necessary to repeat what was then said.

We began five years ago with only the first year of the course organized, with a teaching staff of fifteen, and with an entering class of students numbering eighteen. A year from last October the organization of the entire four years' course was completed, and last June we graduated our first class of fifteen students. During the academic year now closing 167 students have been enrolled as candidates for the degree of Doctor of Medicine, 26 in the fourth year, 34 in the third, 44 in the second, and 63 in the first. All of these are college graduates, and before admission spent a year or more in the study of chemistry, physics and biology. In addition, 69 physicians have been in attendance upon special courses or have engaged in research, making a total attendance of 236. The teaching staff numbers 53, of whom 21 are professors, clinical professors or associate professors. The steady growth of the Medical Department with each succeeding year has, therefore, been most gratifying and has laid to rest the fears, which some at first entertained, that our high standard of admission, necessitating not only a degree in arts or science, but also a good practical training in physics, chemistry and biology, with a reading knowledge of French and German, and acquaintance with Latin, would restrict unduly the number of students.

Not less significant is the national character of this Medical School as shown by the distribution of the students among the several States. 30 are credited to Maryland, but of these a number have made this their home only since entrance into the School. Of the remainder, 32 come from New England, 22 from the Middle States, 27 from the Southern, 38 from the Middle West or Central States, 13 from the West (11 being from Calfornia), and 5 from Canada, Hawaii and India.

47 colleges are represented, the Johns Hopkins University by 31 students, Yale by 29, Harvard and the University of

Wisconsin by 9 each, Wellesley and Smith by 7 each, the Leland Stanford Jr. University and the University of California by 6 each, and Princeton, Williams, Amherst, Vassar, Cornell, the University of Chicago and other colleges by smaller numbers.

But more significant than the growth of the School in numbers or the wide area from which our students are drawn are the contributions to the advancement of medical education in this country which we may fairly claim to have made. The mere addition of a new medical school to an already overburdened list can hardly be regarded as a meritorious act. We have realized from the start that unless we had something to contribute to the promotion of medical education and knowledge, there was no reason for our existence. No one familiar with the conditions of medical education in this country could fail to see that the opportunity existed to do for medical education what this University has accomplished for university education in this country. With the inspiration of such an example and with these high ideals before us, what better place could be found for such a work than in this University and in the city of Baltimore? It would occupy too much time on this occasion to enter into details upon this subject, but concerning two or three of the more distinctive features of this medical school I shall ask permission to say a few words.

We have raised the requirement as to the training preliminary to the study of medicine to a point not only beyond that of any other medical school in this country, which in view of the former low demands in this respect might not signify much, but to one equal to, if not in advance of, that of any foreign university. This high standard of admission, instead of proving a weakness, has been one of the main sources of our strength. It has secured for us students whose average fitness for the study and practice of medicine is unquestionably greater than has been hitherto attained in our medical schools, and it has brought to us not a few of unusual capacity and promise. Students are attracted to an institution where their associations are wholly with liberally educated classmates, and the resulting tone and morale of the School are elevated, in welcome contrast to the traditional conception of the social and moral atmosphere of a medical school. It is evident that far better methods of teaching and better results can be secured with highly trained students than with those without adequate preparation.

While we designate our required period of medical study as four years, it is in reality from five to six years, for we relegate to the period of preliminary collegiate training the study of general chemistry, physics and biology, which are included in the medical curriculum of many schools, especially in Europe. The study of these sciences, which is justly considered to be an essential part of a thorough medical education, can be pursued to greater advantage in a college or university than in a medical school, and the arrangement which we have adopted adjusts itself readily to the existing conditions in our best colleges and universities.

Coming to us with this exceptional training, our students have a right to expect exceptional advantages for the study of the profession which they have chosen, and, so far as our resources permit, we have endeavored not to disappoint them in this respect. The aim of the School is primarily to train practitioners well grounded in the fundamental medical sciences and in practical medicine and surgery and their branches. We have broken completely with the old idea that reading books and listening to lectures is an adequate training for those who are to assume the responsible duties of practitioners of medicine. Anatomy, physiology, physiological chemistry, pathology, bacteriology, pharmacology and toxicology are taught during the first two years by practical work in the laboratory, and in the last two years disease is studied in the dispensary and at the bedside, not merely as it is described in books.

At the beginning we had only one laboratory building; in 1894 we were provided with a second commodious building, the Women's Fund Memorial building, intended for the various anatomical sciences; in 1896, through a generous gift to the Hospital, we were enabled to construct the Clinical Laboratory, and in the coming autumn a still larger building, now in process of erection, will be ready for the laboratories of physiology, physiological chemistry and pharmacology. We shall then be well equipped with the needed laboratories, which constitute the workshops of our students during the first two years of the course.

From these laboratories the students pass at the beginning of the third year directly to the Dispensary and the wards of the Hospital, where our arrangements to enable them to become practically familiar with the symptoms, the diagnosis and the treatment of disease constitute perhaps our most original and valuable contribution to the methods of teaching practical medicine. The generous co-operation of the Trustees of the Johns Hopkins Hospital, in accordance with the wishes of its founder, in rendering available for the instruction of students the resources of this great institution, has placed it in our power to make the years devoted to the training in the practical branches of medicine and surgery peculiarly attractive and efficient. They also provide for a large number of our graduates, as well as to others, opportunities to serve as interns in the Hospital.

The advantages of thus coming throughout the entire course into direct personal contact with the objects of study are not merely that the students thereby acquire a more useful and living knowledge of them, but that they become familiar with scientific methods and acquire something of the scientific spirit of investigation and of approaching medical problems. They should thus be enabled by their subsequent observations and experience to carry on an education, only begun at the medical school, and which should continue throughout their professional lives.

To obtain the best results of practical training of the kind mentioned it is of importance that the student should be brought into contact with those who are not merely teachers but also investigators. In the selection of heads of departments the Trustees of the University and of the Hospital have kept in view that a great medical school should not only teach medicine but also advance the medical science and art. We feel that we may take just pride in the number and value of the published contributions to medical knowledge by mem-

bers of the staff of the School and Hospital, and, indeed, it is a sign of great promise that several of our students have already conducted noteworthy investigations, leading in some instances to important discoveries.

In a school with such standards for preliminary training and with such opportunities and methods of study, it is self-evident that the standard of attainment should also be kept high, so that the bestowal of its diploma may be a real distinction to such as attain it. In this respect the Faculty have felt a serious sense of responsibility, directed solely by the desire that no one shall be promoted to the doctorate of medicine in this University who does not measure up to the high standards which have here been set.

I have endeavored to point out in a few words the lines along which this Medical School in the short period of its existence has developed and certain of its salient characteristics. We feel that we have here an unrivaled opportunity for the development of a great medical school, devoted to higher education and the advancement of medicine. The time is one of marvellous activity and progress in medicine, with new paths and new vistas constantly opening for exploration. We cannot occupy the vast field so fully as we desire. We need ampler resources to take full advantage of our opportunities. I know of no direction in which pecuniary investments for education will yield larger returns in advancement of knowledge and promotion of the welfare of mankind than in the endowment of higher medical education.

Medical departments of universities in this country have usually been such in name only and at best have been looked upon as step-children, out of harmony with true university life and ideals. A medical department which brings to the University only liberally educated men and women, provides a four years' course of study conducted with the best methods, cherishes the scientific spirit and contributes to the advancement of knowledge, is surely a worthy member of a university, however high its ideals. The medical department which has here been founded has been cordially received by this University as equal and coordinate with its philosophical department. This intimate union of Medical School and University is of mutual benefit, and in this close association we find constant encouragement and incentive to attain the best. We have been guided throughout by the unceasing care and wise direction of the President of this University, and we believe that the enlightened and generous policy of the Trustees of the University and the Hospital has brought to fulfillment the wishes of the founder of this University and of the Hospital concerning the Medical School for which he provided.

Members of the Graduating Class:

In behalf of my colleagues and for myself I congratulate you upon the satisfactory completion of a prolonged period of liberal and professional study in preparation for your chosen career.

You, with the class which preceded you, came to us when you could not see plainly the end from the beginning, trusting in assurances held out to you for the future. You have participated in the establishment of this Medical School. This circumstance imparts peculiar interest and intimacy to your relations with us.

It is during this formative period that the impress of students' ideals and conduct upon the inner life of a university is most distinctly felt and that traditions are formed which may powerfully influence the future health and vigor of the institution. That your influence upon this inner life has been for good, we feel assured. During all these four years we have been stimulated by your diligence, enthusiasm, ability and desire for knowledge, and we appreciate your hearty cooperation with our efforts. We, your teachers, have acquired more than a teacher's interest in you. Intimate acquaintance has led to genuine friendship, and we do not doubt that we shall have occasion to feel a personal pride in your future good work. You go forth with the best wishes and high expectations of all of us.

You have acquired some knowledge of the fundamental principles of medical science, some practical familiarity with the nature and treatment of disease and injury, the ability to use the instruments of your profession, and, above all, I trust, correct methods of work and a trained scientific spirit of investigation. Of the entire contents of the science and art of medicine you have, however, learned relatively only a small part, but you are now in position to increase your knowledge through your own individual efforts and through experience to acquire wisdom.

Such a training as you have received should enable you to derive satisfaction of a high order in the pursuit of your profession, a satisfaction not to be obtained from its practice merely as a trade and means of subsistence. The scientific physician of to-day finds intellectual pleasures, as never before, in the study of the science and the practice of the art of medicine, and this scientific interest is dignified and enhanced by the power, ever increasing, of doing good to others through the relief of pain and suffering. To the ranks of this noble and useful profession we now welcome you.

Mr. President:

In the name of the Medical Faculty I have the honor to present to you twenty-two candidates whom we recommend for promotion to the degree of Doctor of Medicine in this University. All, after receiving a liberal education indicated by a degree in arts or science and fulfilling all of our requirements for admission, have spent four years in the study of medicine and have satisfactorily completed the course in this University.

LIST OF STUDENTS RECEIVING THE DEGREE OF DOCTOR OF MEDICINE.

WILLIAM STEVENSON BAER. A. B., Johns Hopkins University, 1894. Baltimore.

WILLIAM JEPHTHA CALVERT. A. B., University of Kentucky, 1893; Graduate Student, Kentucky State College, 1893–94. Lexington, Ky.

PATRICK JOSEPH CASSIDY. A. B., Yale University, 1894. Norwich, Conn.

JOHN WILLIAMS COE, JR. Ph. B., Yale University, 1893. Meriden, Conn.

PERCY MILLARD DAWSON. A. B., Johns Hopkins University, 1894. Montreal, Canada.

ARTHUR WELLS ELTING. A. B., Yale University, 1894. Upper Red Hook, N. Y.

WILLIAM WEBER FORD. A. B., Adelbert College, 1893. Norwalk, O.

THOMAS WOOD HASTINGS. A. B., Johns Hopkins University, 1894. Morristown, N. J.

ALFRED BIRCH HERRICK. A. B., Williams College, 1894. Amsterdam, N. Y.

JAMES HALL MASON KNOX, JR. A. B., Yale University, 1892, and Ph. D., 1894. New Haven, Conn.

MILLARD LANGFELD. A. B., Johns Hopkins University, 1893. Baltimore.

GERTRUDE LIGHT. S. B., University of Wisconsin, 1894. Milwaukee, Wis.

JAMES DANIEL MADISON. S. B., University of Wisconsin, 1894. Mazomanie, Wis.

HARRY TAYLOR MARSHALL. A. B., Johns Hopkins University, 1894, Baltimore.

ROGER GRISWOLD PERKINS. A. B., Union College, 1893, and Harvard University, 1894. Schenectady, N. Y.

KATHERINE PORTER. A. B., Bryn Mawr College, 1894. Baltimore.

JOSEPH HERSEY PRATT. Ph. B., Yale University, 1894. North Middleboro, Mass.

GEORGIANA SANDS. A. B., Vassar College, 1893; Graduate Student, Barnard College (N. Y.), 1893–94. Port Chester, N. Y.

BENJAMIN ROBINSON SCHENCK. A. B., Williams College, 1894. Syracuse, N. Y.

WALTER RALPH STEINER. A. B., Yale University, 1892, and A. M., 1895; Graduate Student, Johns Hopkins University, 1892–94. Baltimore.

EMMA ELIZABETH WALKER. A. B., Smith College, 1887. Parkersburg, W. Va.

ANDREW HENDERSON WHITRIDGE. S. B., Harvard University, 1894. Baltimore.

CONCLUSIONS FROM CLINICAL AND BACTERIOLOGICAL EXPERIMENTS WITH HOLOCAIN.

BY ROBERT L. RANDOLPH, M. D.

I have been using holocain for some months and have recorded here fifty-four cases where I employed it in the eye clinic of the Johns Hopkins Hospital. Seventeen of these cases were foreign bodies in the cornea, and the average time employed to produce anesthesia was a little less than two minutes. In three cases iridectomy was performed, and in eight cases cataract extraction. Here I made the same number of instillations as I do when employing cocain, that is, three in fifteen minutes, and all that can be said is that I noticed no difference in the anesthesia from that produced by cocain, and the same may be said of eight tenotomies. The other cases were where the holocain was employed after the application of irritating substances as copper sulphate, nitrate of silver, and after the passing of probes, in operations for tarsal cysts and pterygia. With the exception of the tarsal cysts the anesthesia was produced in a little more than two minutes.*

Most of those who have reported on the subject of holocain have alluded to its germicidal properties. I have looked through the literature and, with the exception of some very meagre experiments made by Heinz showing that the yeast bacteria are retarded in their growth by contact with holocain, have found no record of experiments proving that a solution of holocain is germicidal.

The following experiments were made to throw some light upon this aspect of the question.

I. To determine the effect of a 1 per cent. solution of holocain upon the micrococcus epidermidis albus (Welch). For this purpose thirty wooden toothpicks were sterilized by boiling for ten minutes. They were then immersed for five minutes in a suspension of the organisms in sterilized water, afterwards taken out and dropped into a 1 per cent. solution of holocain. Here they were allowed to remain fifteen minutes. They were then taken out with long sterilized forceps and plunged each into a tube containing nutrient agar. After being in the thermostat twenty-four hours they were inspected and in every tube there was a luxuriant growth. Control tubes showed that the pieces of wood were sterile before immersion in the suspension of organisms. The growth in half of the tubes was examined and the micrococcus epidermidis albus was found in every instance. Fifteen experiments made with the staphylococcus pyogenes aureus resulted in the same manner. In another series glass rods were employed instead of pieces of wood. The rods were sterilized by holding them in the flame. They were then dropped into a suspension of the aureus in sterilized water and allowed to remain there five minutes. When taken out, instead of putting them directly into the holocain solution as was done in the first and second series, they were put into a sterile tube and allowed to dry thoroughly, and then immersed fifteen minutes in a 1 per cent. solution of holocain, after which each rod was plunged into a tube of nutrient agar. The result was the same as in the first and second series.

II. To determine whether a 1 per cent. solution of holocain has an inhibitory effect upon these same organisms.

Five grains of holocain were dissolved by boiling in 8 cc. of water, and to this were added 24 cc. of fluid agar. The resulting mixture was practically a 1 per cent. solution of holocain. Twenty tubes of "slant agar" were prepared in this way, and ten "smear cultures" made of the staphylococcus pyogenes aureus, and ten of the micrococcus epidermidis albus. These tubes were inspected every day for three days, but there was never any evidence of a growth. This experiment was repeated a number of times by others in the laboratory as a control measure, and in every instance with the same result. Neither the staphylococcus pyogenes aureus nor the micrococcus epidermidis albus would grow in a medium containing holocain in the proportion mentioned. It should be said that these organisms will grow in nutrient agar containing holocain in the proportion of ½ of 1 per cent.

The positive results of the experiments to determine whether

* For an exhaustive account of the clinical aspect of holocain see the various reports of Henry Würdemann, M. D., Milwaukee.

holocain had an inhibitory effect upon the organisms would seem to indicate that some of the organisms on the glass rods and pieces of wood in the first, second and third series were killed. To determine this question the following experiments were made. A thick suspension of the staphylococcus pyogenes albus was made in a physiological salt solution. Five loops of this suspension were transferred to a tube containing 8 cc. of a 1 per cent. solution of holocain, and five loops were transferred to a tube containing the same quantity of salt solution; this latter measure as a control. After allowing the organisms which had been transferred to the holocain solution to remain there five minutes, two loops of the latter solution were carried into fluid agar and plate cultures made. This was repeated after ten, fifteen, twenty and thirty-five minutes, and finally after twenty-four hours. In the first plate (after five minutes) there were fifteen colonies; in the second plate (after ten minutes) there were about the same number; in the third plate (after fifteen minutes) there were five colonies; after twenty minutes three colonies; after thirty-five minutes two colonies and a big impurity, and finally after twenty-four hours the plate was sterile. This series was repeated and with practically the same result. There was a gradual diminution in the number of the colonies the longer the organisms were allowed to remain in the holocain, and after twenty-four hours it was seen that the holocain no longer contained living organisms. Plate cultures made after twenty-four hours from the salt solution showed numerous colonies.*

Conclusions: Holocain, in so far as its anesthetic properties are concerned, seemed in these fifty-four cases to have been sufficiently effective. In those cases where a test was made of the rapidity of its action, as for instance in foreign bodies in the cornea, pterygia, and after the application of irritating substances, the quickness with which anesthesia was produced was striking. Whether the anesthesia produced after two minutes is sufficiently profound to guarantee a painless iridectomy or a satisfactory cataract extraction I did not determine, but in those cases where operations of this character were performed, and where the holocain was instilled just as we do cocain, no difference was observed in the anesthesia from that produced by the latter.

The drying of the cornea and desiccation of its epithelium and the dilatation of the pupil, the absence of which phenomena has been noted by others, have been confirmed by my own observations. The absence of these two properties should recommend it for office use for the removal of foreign bodies, as it is well known that after the employment of cocain in such cases, blurred vision and slight photophobia are often present for hours.

A 1 per cent. solution of holocain has not only an inhibitory effect upon the pus organisms, but these organisms are killed when exposed to a solution of this strength for a certain length of time. No attempt was made to determine the point of time at which these organisms lose their vitality on exposure to holocain, but it may be safely said that this point is somewhere within twenty-four hours. Furthermore, exposure to a 1 per cent. solution of holocain for periods of five, ten, fifteen, twenty, twenty-five and thirty-five minutes showed in every instance a gradually diminishing number of colonies in the plates, so that it is plain, in spite of the luxuriant growth around the glass rods and pieces of wood, many of the organisms were killed.

It may be said in conclusion, then, that a solution of holocain of the strength employed in ophthalmic practice possesses distinct germicidal properties, a fact which it is evident enhances the value of this product.

*It is evident that the amount of holocain brought over in the loops was not sufficient to alter the properties of the agar to the extent of inhibiting the growth of organisms. In order to produce this effect more than ½ of 1 per cent. holocain should be present in a given quantity of agar. Hardly more than two or three drops in all of holocain were brought over in the loops, so the reason, then, that the organisms did not grow was because they were killed before they were transferred to the plates.

OBSERVATIONS ON THE EPITHELIUM OF THE URINARY BLADDER IN MAN.

BY PERCY M. DAWSON, M.D.

The following report deals, first, with the clinical history of a patient treated for urethritis in the genito-urinary dispensary of the Johns Hopkins Hospital; secondly, with the microscopical study of specimens of bladder epithelium obtained from this patient during the course of treatment.

CLINICAL HISTORY.

F. S., male, aet. 23, single, huckster, native of Baltimore.

The patient presented himself at the dispensary on January 6, 1898, complaining of swelling of the left testicle. He gave a history of an attack of gonorrhœa one year ago, and of a second attack which began about December 18, 1897. Of this last attack the period of incubation was nine days. There was considerable ardor urinæ, but only a slight discharge. No other local symptoms and no constitutional symptoms were present. By December 28, 1897, the discharge had become too scanty to be observed by the patient. On January 2, 1898, he noticed a swelling of the left testicle and also tenderness on pressure.

On examination (January 6, 1898), the contents of the left scrotal sac measured 3.5 x 4 x 7 cm., the swelling being chiefly in the globus minor, which was extremely tender on pressure. The skin of the scrotum was red, slightly œdematous, but not adherent. The left cord was slightly enlarged and somewhat tender. Right testicle and cord normal; inguinal glands palpable on both sides, but not enlarged.

The urethral discharge was thick, slightly yellowish and very scanty. It contained a few pus cells and a few cocci

and short thick bacilli which did not decolorize by the Gram method.

The urine was of a pale amber color and slighly acid. In the first glass of the two-glass test the urine was uniformly cloudy, but on standing a small quantity of light, white, flocculent sediment was deposited, leaving only a few mucous shreds in the supernatant fluid. This sediment was found to contain a considerable number of pus cells and a very few epithelial cells. The contents of the second glass were similar except that the sediment was very scanty and contained no pus.

The treatment adopted was the vigorous use of the Paquelin cautery over the affected epididymis, as recommended by Halsted, and for the urethritis intravesical injections of a solution of potassium permanganate, 1: 6000. An order was given for an irrigation apparatus and for permanganate tablets, and the patient was directed to force the solution into his bladder three or four times daily.

On January 10, 1898, the patient returned. The urethral discharge had ceased. The urine showed a diminution in the amount of sediment and in the number of pus cells which it contained.

On January 11, 1898, the patient began to retain the irrigation fluid in his bladder, sometimes for as long as one or two hours, thinking that this might hasten his recovery. This manœuvre was persisted in for two days (January 11, 12), in spite of the fact that the patient experienced a dull heavy pain in the region of the sacrum while holding the irrigation fluid. This pain always disappeared immediately on micturition.

On January 13, 1898, the patient came complaining of these pains in his back and of a sensation of itching on the glans penis. The affected testicle, though still considerably swollen, was much less painful. The meatus looked a little reddened, but there was no discharge. The patient had not emptied his bladder since his last injection at 8 a. m. and it was then 10.30 a. m. The urine when voided was of a peculiar smoky brownish color and contained a number of small brownish flakes which soon settled to the bottom. There was also a considerable sediment composed of such flakes. In the supernatant urine floated about twenty large membranous flakes, of extreme thinness and of a dark brownish color. Several of these flakes were as large as the little finger-nail, one measuring 8 x 12 mm. They hung quivering just beneath the surface of the liquid for some hours before finally settling to the bottom.

On microscopical examination, these bits of membrane were found to consist of a single layer of polyhedral cells, forming a perfect mosaic and entirely intact. The sediment was composed of cell detritus and a great number of epithelial cells, single or in groups, some well preserved, others more or less decomposed or necrotic. No pus was observed and no blood.

The contents of the two glasses were similar, except that the first contained a larger quantity of sediment.

The patient was directed to continue the use of the permanganate solutions, but not to retain them in the bladder.

All this was at 10.30 a. m. At 1 p. m. the patient irrigated himself, but on expelling the fluid observed nothing unusual. At 4.30 p. m. he made the same observation. At 8.30 p. m. he came to the hospital and voided there perfectly normal urine, in which neither pus cell nor epithelial cell could be demonstrated even after centrifugalization.

Subsequently the patient returned to the dispensary several times. His last visit was on January 31. He assured us that he felt perfectly well. He had been away from home since January 17 and had irrigated himself only four times during the past two weeks.

The left globus minor was slightly larger than the right (which may have been normal) and was not at all tender. There was no discharge. The urine was amber, slightly cloudy, with one or two shreds in each glass. On standing, a small amount of sediment was deposited in the first glass, which on examination was found not to contain pus cells.

MICROSCOPICAL EXAMINATION.

The specimens obtained from the patient, F. S., consist entirely of surface epithelium. They were fixed and hardened, some in sublimate, others in absolute alcohol, and were stained with saffranin or by the iron-hæmatoxylin method.

The larger cells are irregular and polygonal in form; the smaller ones are often hexagonal. Their outlines are very clear. Along the margins of many of the cells is a row of short teeth-like processes which seem to bind together the adjacent cells. They resemble the intercellular protoplasmic bridges described by some authors, but from our preparations their exact nature cannot be determined.

The granular protoplasm usually fills the entire cell, but sometimes, especially in the larger cells, there is a clear non-granular zone in the periphery. In the cells in which the finer structure can be made out, the cell body appears to be composed of countless minute vacuoles, between which the protoplasm is uniformly granular. In some cases the whole cell body appears homogeneous, but usually this vacuolated structure can be observed.

The nucleus is round or oval, sharply outlined, and situated at or near the centre of the cell. The chromatin is diffused throughout the nucleus, and also concentrated into several dark irregular masses about five to fifteen in number. With careful focusing connecting bands between these masses may sometimes be found, resembling somewhat a nuclear figure composed of several moniliform chromosomes knotted and coiled together.

In many instances vacuolated nuclei were found. There is rarely more than one vacuole in a nucleus. They are usually central, and the chromatic masses are displaced and lie upon the surface of the vacuole.

In the protoplasm of many of the cells vacuoles can be seen, some quite small, some so large that the nucleus is crowded to the periphery, the whole cell being swollen and presenting the signet-ring appearance so characteristic of fat cells. Between these extremes all sizes of vacuoles and all degrees of nuclear displacement occur.

The most striking phenomenon observed in the study of these cells is the budding of the nuclei. In some cases the buds occur as knobs upon the surface of the mother nucleus; in others they are attached to the mother nucleus by a pedicle containing a chromatic material which may be either short and broad or may appear as a fine uniting band. Or again, the bud may be free in the cell protoplasm, and in such cases it is only

their small size which suggests their origin. The larger buds contain one or more masses of chromatin; the smaller ones usually do not. The varieties of these budding forms are almost innumerable. There may be one to four buds each varying independently of the others in size and in the manner of their attachment, so that examples of all stages of this process occur in abundance.

In addition to the cells with budding nuclei there are many multinucleated cells, and the rarity with which one finds the nuclei dividing into equal daughter nuclei, and the fact that between the nucleus with a little broken-off bud and the binucleated cell every gradation exists, strongly suggests that the multinucleated cells are derived from the mononucleated by a process of budding.

There is a class of cells of which examples are frequently found. They differ from those above described in being larger, with one or two larger and paler nuclei which are sometimes irregularly fragmented. These may be cells which have become swollen and degenerated either before the budding process had begun or perhaps just after the first division of the mother nucleus.

Not only do cells with two nuclei occur, but we also find them with three, four, up to huge giant cells with fifteen nuclei. As a rule the nuclei of these giant cells stain more feebly than do those of the mononuclear cells. The protoplasm is somewhat more granular, the clear zone bordering the periphery is often very marked, and the surrounding cells often appear to bulge into them. The protoplasm is often vacuolated, and in some, one or more of the nuclei are found budding.

To give some idea of the frequency of the budding and of the multinucleated forms, a differential cell count was made. In an area which under the low power did not appear particularly promising there were in 1000 cells—

70 cells with 1 bud,
15 " " 2 buds,
5 " " 3 "
3 " " 4 "

93 cells with budding nuclei.

Also 40 cells with 2 nuclei,
3 " " 3 "

43 multinucleated cells.

And in another area where the giant cells were abundant there were in two adjacent fields of the $\frac{1}{12}$ oil immersion—

5 cells with 2 nuclei,
3 " " 3 "
2 " " 4 "
1 " " 6 "

LITERATURE.

The literature on the structure of the bladder mucosa appears to be very scanty. Our text-books on histology are almost silent on the subject, and it was only in an article by Dogiel that a detailed description has been found.

In 1890, A. S. Dogiel, professor of histology in the University of Tomsk, published in the Arch. f. Micro. Anatomie an article entitled "Zur Frage über das Epithel der Harnblase."

In his study of the epithelium Dogiel employed paraffin sections and macerated preparations of the bladders of the house mouse, white mouse, rat, hamster, cat, dog, and man.

He describes the epithelium as being composed of four layers: the first consisting of squamous cells; the second of cuboidal, columnar, and pyriform cells; a third layer similar to the second; and the fourth layer of round or fusiform cells filling up the interstices between the cells of the third layer.

The cells of the first layer resemble thick plates. They are irregular, polygonal, and sometimes divided into two parts by a central constriction.

The protoplasm of the cell usually consists of two more or less distinct parts—an upper and a lower. The upper is one-third the whole thickness of the cell, homogeneous or only slightly granular, and stains red with picro-carmine. The lower part is very granular and stains yellow with picro-carmine. The granular appearance is due to a network of rather thick fibres, between which is a clear interfibrillar substance.

On the under surface of the cell one finds rather deep depressions. They are from three to ten in number, depending upon the size of the cell. Into these depressions fit the upper ends of the cells of the second layer. From the bottom of each of these depressions several canals of various calibres arise and run towards the upper surface of the cell, passing almost completely through the granular layer. These canals have usually an oblique direction and end blindly. They are continuous with the cup-shaped depressions on the under surface of the cells. They contain protoplasmic prolongations arising from the underlying cells, which, together with protoplasmic threads hanging down from the cells of the superficial layer, intimately unite the cells of the two layers. These canals and protoplasmic threads are conspicuous in the mouse and rat, but are poorly developed in other animals.

On the superior surface of these cells one often finds one or more nodular, polypoid or sausage-shaped projections composed of a granular material. These granules may be regarded as being of a mucous character, for they bear a close morphological resemblance to mucous granules and stain intensely with hæmatoxylin. Hence the whole surface of the bladder may be regarded as a spread-out mucous gland.

In the granular part of each epithelial cell lies the large vesicular nucleus, round or oval in shape, and surrounded by a rather thick membrane with a double contour. In some cases vacuoles occur in the nuclei.

The nuclear network is composed of threads of varying thickness running from the center to the periphery. In each nucleus occur two to fifteen round, oval, or rod-shaped granules, one usually being larger than the rest. They stain much more deeply than the rest of the nucleus and sometimes appear to have a bright border.

Of these nuclei there are present in each cell one to twelve or more. The multinucleated cells are quite abundant in the small rodents, while in the cat, dog and man this is not the case. The nuclei may be in one or more groups, or scattered, or in pairs and biscuit-shaped. In size these nuclei vary greatly. There may be a number of equal nuclei, or one nucleus may have a number of smaller nuclei clustered about it, forming a sort of colony.

One often meets with nuclei which are constricted by a circular furrow, sometimes of such a depth that the two parts of the nucleus are united by only a slender band. In many cases there are two or more such furrows. The parts into which the nucleus is thus divided vary greatly in their relative sizes, and hence the variation in the size of the nuclei of the multinucleated cells.

Throughout this division the nuclear membrane remains perfectly distinct and there is no observable change in the chromatin. Hence we have to do with a process of amitotic division, or rather of budding.

As to whether or not the division of the nucleus is followed by a division of the cell body, Dogiel is unable to decide, but merely remarks that the occurrence of constricted cells favors the view that such division does occur.

The remaining layers of the mucosa concern us but little. Their cells increase by a process of mitosis and not by budding. In the rodents the cells of the second layer are brought into intimate relation with those of the first layer by means of the protoplasmic processes above mentioned.

Conclusions.

It will be observed that the description of the cells obtained from the urine of the dispensary patient agrees in part with the description given by Dogiel. There are, however, some noteworthy differences.

In these specimens no stellate arrangement of the chromatin is present, nor any pale ring surrounding the masses of chromatin, nor is there any tendency for one mass of chromatin to exceed the rest in size. There is no cupping of the under surface of the cells, nor any sausage-shaped projections from the upper surface.

Dogiel makes no mention of the "bridges" between the cells of the superficial layer, while on the other hand our specimens do not show the canals and threads which Dogiel describes as being so well developed in the small rodents but so poorly developed in the larger mammalia. In our specimens, the absence of these connecting threads and the existence of the cell bridges may explain the occurrence of the large flakes of mucosa, the connections between the individual cells of the superficial being so much stronger than the connections between this layer and the one below it.

That there is any protoplasmic network of rather thick fibers, such as Dogiel describes, these specimens afford no evidence at all. Whenever any finer structure can be made out, the cell body is seen to be composed of vacuoles with a uniformly granular protoplasm between them.

Of the occurrence of the giant cells, Dogiel says that they are common in the small rodents but rare in man. In these specimens of human bladder, however, there is quite a different state of things, as the result of the differential cell count shows.

What is the significance of this formation of giant cells? Is it a simple process of proliferation, as Dogiel thought, or is it a process, so to speak, of slow and orderly fragmentation? The specimens have furnished not the slightest evidence that this is a true cell division and not merely a nuclear division, for in no instance have cells been found having a central constriction of the protoplasm such as Dogiel has described. It is not probable that the weak solution of potassium permanganate produced any particular change in the cells. The giant cells contain large vacuoles much more often than do the mononuclear cells, their nuclei usually stain more feebly and are more often seen to be fragmenting irregularly. All these observations, namely (1) the absence of cell division, (2) the deficient nuclear staining, (3) vacuolization, (4) karyorhexis, point to the fact that we have to do with a process of degeneration.

In conclusion I wish to thank Dr. Young for the permission to report the case, and for the interest he has shown in the study of the specimens.

Fig. 1.—*a*. Nucleus with two buds.
b. Large pale nucleus with bud.
c. Nucleus with vacuole.
d. Nucleus dividing.
e. Cell with two nuclei
f. " " three " (near center of field).
g. " " four "
h. " " five "
i. " " ten "
j. " " vacuole.
k. Giant cell with vacuole displacing nuclei.
l. " " " degenerated nuclei and vacuolated protoplasm.

Fig. 2.—Shows single cells with "teeth-like margins," and more or less distinct vacuolization of the protoplasm.
a, *b*, *c*. Cells with one, two and three nuclei respectively.
d. Cell with nucleus in process of division.
e. Cell with three nuclei, of which one has a large and a small bud.

Discussion.

Dr. Barker.—We are to be congratulated upon having this case so thoroughly worked up. It is curious that the epithelium is shed in such large sheets. It looks as though the cement substance connecting the superficial layer with the parts below is more susceptible to attack by the permanganate solution than that between the individual cells of the superficial layer. I have had the opportunity of studying these specimens with Mr. Dawson and have been much interested in many of the pictures he has obtained. The number of giant cells present is surprising. It is important to determine whether or not as many as he finds are normally present, that is to say whether or not the permanganate solution has actually caused an increase in the number of these cells. There is some evidence that these giant cells of the bladder wall may play a part in pathological processes. The late Dr. Brown once showed me a section from a carcinoma of the bladder in which there were large numbers of such multinucleated epithelial giant cells.

It would be easy to continue the study by animal experiment, and I would suggest if it should turn out that water alone is incapable of causing the changes described in the bladder, that an attempt be made to determine just what constituent of the permanganate solution it is that is active, the cation, the anion, or the non-dissociated molecule. It would seem probable *a priori* that the anion is the constituent concerned.

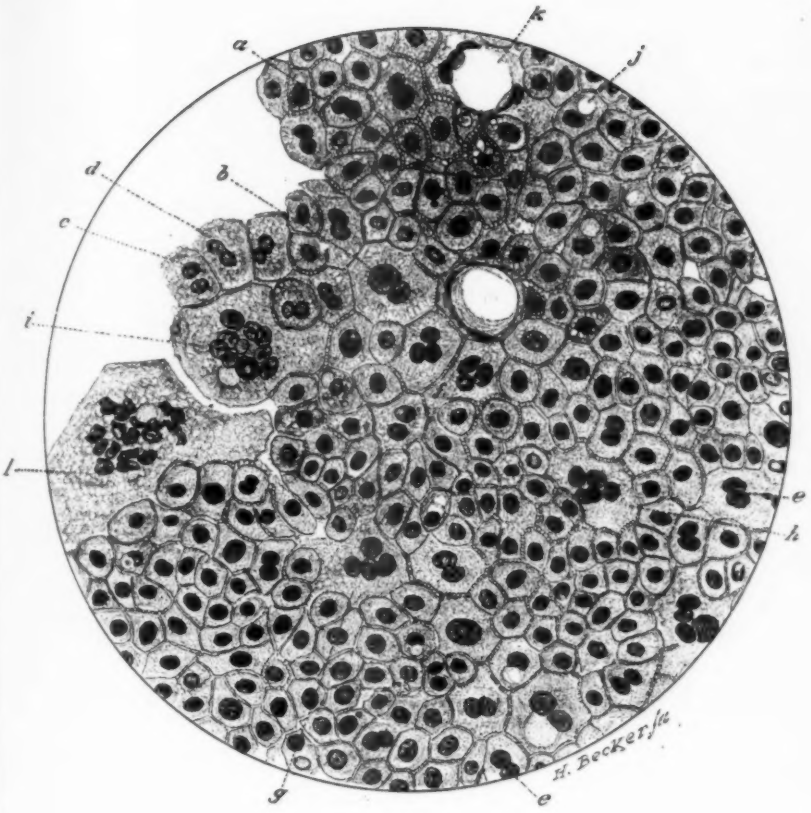

Fig. 1.

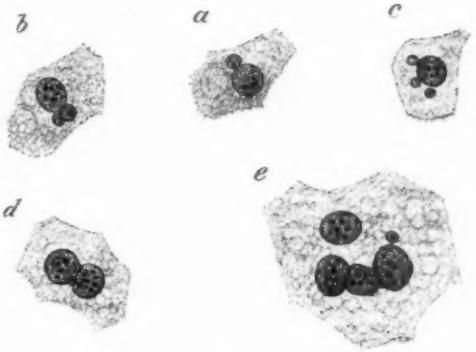

Fig. 2.

Dr. THAYER.—I saw some of the specimens and I would like to call attention to the great similarity of some of the pigment of the nuclei to that of some of the blood corpuscles in grave diseases. In the blood there can be very little doubt that it is a karyolitic process.

Dr. OSLER.—It would be very interesting to have Mr. Dawson study the epithelium of the bladder in a series of post-mortem cases. I think he would probably find a very large number of these giant cells with many nuclei.

Mr. DAWSON.—Dogiel used two methods, that of cutting sections and that of maceration in various fluids. He does not mention having obtained by the latter method any large flakes of mucosa, but he does describe the single cells obtained in this way.

A CASE OF SARCOMA OF THE ŒSOPHAGUS.*

BY L. E. LIVINGOOD, M. D., *Associate in Pathology, Johns Hopkins University.*

Through the courtesy of Dr. Frank R. Smith I have to present this evening a specimen obtained at autopsy from a patient who died of sarcoma of the œsophagus.

On July 6, 1897, H. S., a German by birth, cabinetmaker, æt. 55, was admitted to the Johns Hopkins Hospital complaining of difficulty in swallowing and "rheumatic pains," especially in the shoulder.

From careful notes taken by Dr. McCrae I have made the following abstract:

"Family history negative. He has been an active, healthy man; denies venereal infection; takes beer moderately, a glass of whiskey regularly in the morning; his work is done indoors. He has lived in Baltimore 15 years; has had rheumatic pain at times during past two years.

"About April 1, 1897, he began to complain of pain in the throat in the neighborhood of the sternal notch. The onset was gradual, and at first the pain was not constant, the patient attributing it to having caught cold. The pain was increased by swallowing, and there developed difficulty in swallowing solids, especially bread. The pain on swallowing seemed to begin at the sternal notch and to extend to the stomach. It persisted only for a few moments. The pain in the neck, however, was constant and was sometimes severe enough to keep him awake. Sometimes on swallowing the pain would run up to both ears, not infrequently bringing tears to his eyes.

"The appetite has been fairly good. No regurgitation of food, no vomiting, no cough, no expectoration, no shortness of breath; bowels regular. He has lost 30 pounds in the last 3 months, but does not think he has lost any strength. No increase of pain on deep breathing, no interference with respiration. Patient was able to keep at his work until July 3rd, nearly 3 months after the symptoms were first noted."

"On admission. Fairly well nourished. No emaciation. Color fair. Puffiness under the eyes. Sclerotics somewhat injected. Pupils equal. Tongue coated, edges red and indented. Gums and mucous membrane of mouth of a fair color. No mass to be felt in the neck. No tracheal tugging. No marked pulsation. Thorax: large and muscular. No pulsation seen or felt. Expansion poor. Respiration largely abdominal. On percussion the note seems clear; possibly there is slight relative dullness behind on the right side in the interscapular region. Breath sounds clear. Heart sounds appear clear, second sounds strong. Pulse strong, synchronous and of equal volume in radials and femorals. Well marked dermatographia. No general glandular enlargement. Soft tube passed into stomach easily, no obstruction." It may be noted that before entering the hospital patient was seen in the dispensary and an attempt to pass a stomach tube was made. Just before entering the stomach it seemed to meet with an obstruction; patient became very much distressed; the tube was withdrawn and a little blood was seen upon the end.

On July 12th the following note was made:

"Stomach tube meets with no obstruction where patient complains of pain, but when passed 44 cm. from the lips there is some resistance to passage of tube. Pressure on tube causes pain. Small amount of bloody material was removed on the point of the tube, but on microscopic examination was found to consist of red blood cells, pus and squamous epithelial cells. No fragments of tissue found.

"The blood examination showed hæmoglobin 88 per cent., red cells 5,040,000, whites 7500. Urine practically normal (3 exms.). On one occasion a faint trace of albumin was found and one hyaline cast. No diazo reaction. No sugar. Specific gravity 1018. The temperature ranged between normal and 101° F. Patient was discharged on July 17th, improved, especially in regard to the rheumatic pains."

From this time on he was seen occasionally at his own home by Dr. Smith. His condition varied a good deal. At times he felt a little stronger and seemed to gain slightly in weight. At other times he complained of great pain and was unable to swallow anything but the smallest quantity of liquids. With the latter he often had great difficulty. For several days at a time he could hardly take any nourishment and complained of a severe cough and pain. On more than one occasion after severe coughing he brought up fragments containing mucus and what looked like necrotic tissue and blood. One specimen of this was examined under the microscope, but it was too much decomposed to give any clue as to the nature of the disease. However, the existence of a new growth (probably carcinoma) was strongly suspected. For several days after coughing up this material, patient's condition was materially improved. He could take liquids easily, and even partially solid food could be swallowed. About four days before his death he was suddenly seized with intense

* Read before the Johns Hopkins Hospital Medical Society, May 16, 1898.

pain over the lumbar region and between the shoulders. The abdomen was much distended and was tympanitic. It was not, however, very painful and the distension disappeared in the course of a day or so. After this the patient sank almost into a state of collapse, but occasionally revived and said that he felt much better. He finally died on the 26th of November, 1897, at 4 P. M.

Autopsy at 9.30 P. M., 5¼ hours after death.

Body of strongly built man. Very much emaciated. Skin of sallow hue. Body still warm. Small amount of deep yellow fat. Abdominal cavity shows nothing abnormal.

Thorax.—Lungs voluminous. Left pleural cavity free from adhesions. Right pleural cavity obliterated over lower lobe posteriorly by recent adhesions which can be readily broken up. Left lung shows congestion in posterior portions. Right lung: Anterior and upper portion pale and slightly emphysematous. Upper lobes somewhat puckered and at one point bound by fibrous adhesions to ribs. A few fine adhesions between the middle, upper and lower lobes. On freeing the lower lobe the lung tissue about the root and posteriorly is torn, and a foul-smelling necrotic material escapes, the last part of which is more fluid and smells sour. The lower lobe is large, firm and congested. The serous surface from which the adhesions spring is roughened and hæmorrhagic. About the place where the lung has been torn on removal the tissue is much discolored, soft and necrotic. On cutting the lung loose from its root a cavity communicating with the œsophagus is opened up, from which more sour-smelling turbid fluid pours. The lung in this portion is soft and discolored, and in it there is a gangrenous cavity which could contain several ounces of fluid. The lobe (lower) around this gangrenous area is irregularly consolidated, the consolidation affecting the posterior inferior two-thirds of the lobe. On section the surface in this area is deep red, slightly elevated, dry or granular. The lung is completely airless. The bronchi in this portion of the lung are congested and contain a purulent discolored material. The middle lobe is normal. The upper lobe contains an encapsulated calcareous nodule.

The pericardial cavity normal. The heart is of moderate size. The wall is rather soft and pale. Surface of section is dry. Endocardium normal. Slight atheroma of aorta just above valve. The spleen weighs 250 grams. Condition described as that of acute spleen tumor. Kidneys are large, each weighs about 220 grams. They were in condition of cloudy swelling with congestion of glomerular capillaries. Liver large; condition of cloudy swelling. No evidence of tumor metastases. Other abdominal organs were normal.

Description of Tumor.—About 4 cm. below the bifurcation of the trachea the lumen of the œsophagus is obstructed by a new growth, made up of a main body with several smaller polyp-like masses extending down from it. The main mass presents a thick circular ridge arising abruptly from the mucous membrane of the œsophagus and almost completely encircling a crater-like central portion. It measures about 6 cm. from the upper to the lower edge. It does not entirely surround the lumen of the œsophagus, but leaves a strip of mucous membrane about 2 cm. wide running vertically between its lateral adjacent edges. This thickest part of the mass representing the upper portion of the ridge projects about 1.5 cm. into the lumen, and overhangs the mucous membrane. Its edge is quite regular, sharply defined from the mucous membrane, although the latter is reflected for a short distance upon it. The surface is smooth, rounded, nodular, yellow-white in color; its inner surface, representing the wall of the depressed center, becomes more and more discolored and necrotic. The crater in the center is partially filled with foul-smelling purulent material and shreds of necrotic tumor tissue. The floor is discolored, necrotic, soft and friable, and in the lowest part is continuous, through a short fistulous opening several cm. in diameter, with a gangrenous cavity in the right lung. From the lower end the new growth is seen invading the mucous membrane without much elevation, at first uncovered by epithelium, later projecting beneath the epithelium as a very slightly elevated spur.

This main mass of the new growth extends to within 4.5 cm. of the cardiac orifice of the stomach. Growing down from it for a distance of 1.5 cm. and projecting still further is an elevated irregularly formed polyp-like mass, about the size of the last two phalanges of the little finger, from which a second polyp projects into the lumen. This mass also arises abruptly and regularly from the mucous membrane which is reflected for a short distance over it. Its surface is smooth, white or slightly discolored. The smaller projecting polyp has become necrotic and is quite readily friable. The line of continuity between the two main masses is plainly evident. There is a small nodule the size of a small bean in the muscularis of the œsophagus, about 4 cm. above the main tumor mass, apparently quite distinct from it, although the wall of the œsophagus between them is thickened. This nodule is only visible on section of the wall.

These tumor masses are uniformly firm, elastic, and not friable except in those places in which necrosis has occurred. The surface and edges are smooth, with no appearance of vegetation or excrescences. The surface of section of the periphery of the tumor, when the œsophagus is cut open, shows a shining, uniform, white or slightly pink, moist appearance. It is made up of delicate circling strands of tissue. The mass is subdivided into small nodules by strands of more vascular tissue, extending upwards here and there from the muscularis. No juice can be squeezed from the cut surface. Its surface is somewhat discolored towards the central portion, which is friable, discolored and necrotic, and which penetrates deeply into the wall, and at one point entirely through it. The inner muscular layer of the œsophagus seems to be involved in the new growth, and small areas of new growth appear in the outer muscular coat.

At the upper limit of the growth the muscular wall, mucosa and submucosa, become rapidly normal, showing that the tumor is not infiltrating the wall, as a carcinoma would naturally do.

In the lower polyp the new growth seems to rest upon the inner muscular coat and to be continuous with it. The surrounding tissues are more congested than normal portions, and more congested than the tumor tissue.

The œsophagus is slightly distended above the mass. Its mucous membrane is congested and discolored, having a

green-gray appearance for several cm. above and below it. The external fibrous coat is greatly thickened. Its outer surface is roughened. Corresponding to the central part of the tumor, several pea-sized nodules, which on section are seen to be practically continuous with the tumor tissue, project from the surface. One of these, which is yellow and opaque, is readily broken into and appears to form the floor of a necrotic crypt. To the right of this point the right lung is closely adherent to the œsophagus. Its substance here is gangrenous, of a green-black color, soft and friable. The adjacent portions of the lung are deeply congested. At the point of perforation the lung substance has disintegrated, and there has been formed an irregular gangrenous cavity filled with putrid material. The main bronchi, which run to and through this portion of the lung, contain a blood-stained gangrenous material. Their walls are deeply congested, but are intact. The bronchial lymph glands are diffusely pigmented, enlarged and congested, but careful study shows that they are not infiltrated. A small lymph gland is found lying in the outer wall of œsophagus which is apparently normal.

Bacteriological Examination.—Cover-slips from lung (consolidated area) showed: (1) a number of typical capsulated forms of a lancet-shaped diplococcus; (2) long slender bacilli with pointed ends; (3) a shorter form of thin bacillus, staining irregularly. The diplococcus forms were subsequently isolated in pure culture and identified as diplococcus lanceolatus. The bacilli failed to grow under aërobic conditions. Cultures taken from the spleen and liver were negative.

Microscopic Examination.—Sections cut from a number of points in the tumor show it to be rather uniform in its structure, made up of a tissue rich in cells, often arranged in whorls, but not with distinct alveolar appearance. The deeper portions of the tumor are the most cellular, the superficial portions gradually become necrotic and the cells are separated by wider intervals, giving the appearance of œdema.

The cells are of *spindle shape*, varying in size, usually rather large, surrounded by more or less intercellular substance. The nuclei of the cells are of two distinct types, both elongated and vesicular. One type is small, more deeply staining and irregular; the other is large, pale, sometimes greatly swollen. This latter type of nucleus is usually closely intermingled with the smaller type throughout the tissue. At one place, however, these nuclei seem to lie concentrically placed about a small space and are hemmed in by a zone of cells of smaller type. These larger cells resemble the endothelium lining the tissue spaces and vessels; the smaller represent the fibroblasts of young connective tissue.

The tissue is vascular. The fully formed blood-vessels of the mucosa and submucosa have persisted and lie in deeper parts of the tissue. In the younger parts the blood-vessels consist of a single layer of endothelium, often without even the appearance of a basement membrane separating them from the tissue elements.

For the most part the tumor lies on the muscularis, having infiltrated the submucous and mucous coats, and projects as a group of polyp-like nodules into the lumen of the œsophagus. At the lower margin the transition from normal tissue of submucosa to the cellular tissue of the tumor is quite abrupt. Here the new tissue seems to spring from the muscularis or submucosa. It lies directly on the muscular layer, while strands of muscle tissue project upwards into it.

About the middle of the tumor the new tissue cells have infiltrated in masses and strands the muscularis, and extend down even into the thickened fibrous tissue layer. At a point near the perforation the layers of the œsophagus are seen to be infiltrated, but owing to the great thickening of the fibrous sheath the new growth does not completely penetrate the œsophagus at any point.

Just above the tumor the normal tissues of the œsophagus are very much indurated. There is marked proliferation of small round cells, which are arranged in groups running longitudinally in the mucosa under the epithelium and along the blood-vessels.

A line of union between the main mass and small nodule lying in submucosa above cannot be traced; the small mass seems to have had a separate origin. For a short distance at the periphery the epithelium of the mucosa covers the surface of the new growth, but it soon becomes desquamated.

The surface of the mass is almost everywhere necrotic. Approaching the surface the nuclei stain more and more feebly and the tissue about them becomes œdematous. There is swelling and fragmentation of nuclei. At the edge the nuclei fail to take the stain. Usually there is no polymorphonuclear cell infiltration on the surface.

At some points beginning necrosis is indicated by more marked changes in cells. The nuclei become greatly swollen and contain deeply staining globules of their chromatic elements; this enlargement and hyperchromatosis is a common appearance. Sometimes a cell will contain 2 to 3 large swollen vesicular nuclei, about which there will be a distinct zone of protoplasm staining deeply in eosin. In the lower part the tumor shows most extensive degeneration and is infiltrated with polymorphonuclear leucocytes. The surface is covered with bacteria.

The wall of the perforating sinus extending through the outer wall of the œsophagus *is not lined with sarcoma tissue*, but with necrotic, fully formed fibrous tissue, very vascular, congested and infiltrated with leucocytes, red blood corpuscles and bacteria. This fact indicates clearly that the tumor did not come from the outside nor did it completely penetrate the œsophagus. The penetration was due to destructive action of bacteria which found lodgment in the crypts formed by breaking off of necrotic masses.

Sections stained with polychrome methylene blue show a number of "mastzellen" scattered through the tissues, and occasionally where the tissue is especially cellular, a few "plasma cells" of Unna grouped about blood-vessels. They can have little to do with tumor formation. It appears most probable that the tumor took its origin from the submucosa, growing in form of a polyp, and that all the connective tissue elements of the part entered into its formation. The tissues were fixed in formalin, hardened in alcohol, and stained with hæmatoxylin and eosin, picric acid, fuchsin, and polychrome methylene-blue.

Although the tumor appears of rather benign type of sarcoma, the presence everywhere of karyokinetic figures in cells indicates, aside from the clinical history, that its growth was rapid. These evidences of proliferation were not more marked at the points of contact with the normal tissues than near the necrotic surface, and usually there was appearance of but little reaction on the part of tissues adjacent to either tumor tissue. From this one may assume that the direction of growth was not so much into the surrounding tissues as into the lumen of the gullet. There was no evidence of proliferation of muscle nuclei, and nothing which indicated vascular origin for the tumor except the occasional concentric arrangement of the larger endothelial-like cells.

The literature on sarcoma of the œsophagus, strictly speaking, is very meagre, although text-books on special pathology mention its occurrence. Virchow mentions it in a group with others. Sarcoma of the pharynx, on the other hand, is not uncommon. It is not improbable that this apparent rarity is due to a lack of careful histological study

of tumors arising in this part, where carcinoma is of such frequent origin as to throw one off his guard. Clinically and even on macroscopic examination these two can appear in the same guise. Under certain conditions it may be mistaken for a fibrous polyp.

In the first thousand autopsy records of the Johns Hopkins Hospital primary carcinoma of the œsophagus occurs 11 times, whereas this is the first primary sarcoma noted arising in that part.

In 1877 S. H. Chapman reported a case, which may be included here, of sarcoma of the inferior constrictor of the pharynx and inlet of the œsophagus. The patient was a woman, aged 45. No family history of new growth. No distinct evidence of trauma. Had symptoms of increasing dysphagia during one winter. Died of exhaustion.

Wall of œsophagus was thickened like an inverted cone. On right side of œsophagus, in midst of densest tissue, a cavity communicated from lumen of œsophagus with body of a tumor lying apparently outside, closely adherent to œsophagus and an enlarged gland. The structure of tumor is described as "alveolar." To the right and in front of the carotid artery was another larger gland measuring 1 x 2 inches of alveolar structure, enclosed in dense wall and containing some sero-purulent fluid. Cells of the tumor were mostly spindle cells and large oval granular cells which had formerly occupied the alveoli made by interlacing fibrous tissue strands. The new tissue involved, in some places, mucosa, submucosa and muscularis, and consisted almost entirely of spindle cells, although an earlier stage, of round cells, was observable. No involvement of pharyngeal glands; no secondary deposits anywhere. Chapman believed that the tumor began in the cellular tissue in the inlet and spread upwards and downwards in the wall of the œsophagus.

In the Transactions of the Pathological Society of London three cases are to be found. The first reported by Targett, which the author states is the very first to be reported to that venerable society, occurred in a man of 70. The patient had suffered for three months with much pain between the shoulders and with difficulty in deglutition. He had physical signs of lobular pneumonia in both lungs. The tumor mass, which was attached to the outer wall of the gullet, measured 4½ x 2½ x 1½ inches. Its upper border was just opposite to the bifurcation of the trachea and extended downwards nearly to the cardia. The œsophagus was dilated at the site of the growth, which here was moulded in the form of a tube. The tumor sprang from the submucosa. The muscular coat was free from infiltration except at one spot. The mucous membrane could be traced for a short distance over the upper and lower ends, but on the free surface it had been destroyed by ulceration and sloughing of the tumor itself. The tumor looked white, was uniformly succulent and resembled an "encephaloid cancer." Histological examination showed "small round spindle and tailed cells, some of the latter being very large and containing four nuclei." The spindle cells were arranged as bands and ran in all directions. Some parts resembled myxomatous tissue; no secondary growths.

Shaw recorded a case occurring in a woman of 38. She had suffered from dysphagia for several months, was unable to take her food and became rapidly emaciated. The growth consisted of an ulcer with well defined raised edges encircling the œsophagus. In front it extended up to within one inch of the cricoid cartilage and measured vertically three inches. For the most part the ulcer had merely destroyed the mucous membrane, but in front it involved all the coats and had perforated the trachea a short distance above the bifurcation. Some neighboring lymph glands had been enlarged by the deposit. Microscopically the œsophagus was found infiltrated by a sarcomatous growth consisting of round and oval cells. Secondary deposits were found in the lungs and kidneys. The committee chosen to examine the specimen reported that "The cells are too large for a lympho-sarcoma, nor has the stroma the typical disposition seen in that form of tumor."

Rolleston's case occurred in a man aged 54, who for seven months had suffered from difficulty in swallowing. Two months before he died there developed a painless tumor in the left hypochondrium. Cause of death, lobular pneumonia.

The œsophagus for the lower three inches was narrowed and thickened owing to the presence of a firm growth which completely encircled the lumen. The mucous membrane had ulcerated over the greater portion of the surface of the growth. The growth was adherent to the pericardium, but had not penetrated it. It was firmly united to the right lung. In the upper part of the structure there was a fistulous passage through the growth leading into a gangrenous cavity in the lower lobe of the right lung. The lower lobe was solid, gray in color and œdematous. Several of the glands on the root of the lung were swollen and infiltrated. The whole naked-eye appearance was that of an epithelioma of the œsophagus. Microscopically, the narrow part of the œsophagus was found infiltrated with a growth composed of medium-sized round cells. Towards the edges the growth was seen to begin in the submucosa and to pass underneath the mucosa and outwards into the muscular coat, which was extensively but irregularly infiltrated with nodules of new growth. No alveolar arrangement was noted, except when tumor was invading muscle tissue. There was a fluctuating tumor, very vascular, the size of a man's fist, growing from and displacing the lower ribs on the left side. In the right iliac and in the middle fossa of the skull, and on the first and sixth ribs, and in the lymph glands, vascular soft tumor masses were found, the cells of which resembled those present in the tumor of the œsophagus. Rolleston considers that the growth must have been primary in the œsophagus, judging from its position and its density.

Oppenheimer's tumor seems to have reached the œsophagus by direct invasion from the outside. From his description one is led to believe that he was dealing with an aneurism of the œsophageal artery with an organizing lamellated clot.

From a study of the few reported cases it appears that clinically there is no essential difference between these growths and carcinoma occurring in the œsophagus, and a diagnosis must depend upon those features which indicate the presence of the latter. Age and sex will not distinguish them; they are both incident to more advanced life. The ages correspond very closely to those given by Orth for carcinoma: 40 to 70

years. They occur more frequently in males. The advance, however, of the sarcomata is always rapid, and duration of illness after first appearance of symptoms does not extend over nine months. The factors of causation which are invoked for carcinoma and sarcoma generally, are hidden in these cases.

The symptoms of progressively increasing dysphagia, associated with painful deglutition, exhaustion and cachexia, are common to both.

The partial relief of dysphagia after the discharge of a necrotic mass was noted in one of these cases. Microscopic examination of such a mass might reveal the exact nature of the growth.

The occurrence of wide-spread metastases is apparently as infrequent as is carcinoma, and the localization of these metastases is not more definite.

The more frequent immediate causes of death from sarcomata, too, are exhaustion, with terminal lobular pneumonia or perforation, occurring in one case into the trachea, and in two cases into the lung followed by gangrene of the organ.

With the few cases at command and the abridged descriptions one cannot make more than a provisional statement as to the types of sarcoma most frequent in the œsophagus, their point of origin and their position.

Presumably three of the tumors are of the same type, spindle cell sarcomata, in Shaw's, Targett's and our own; although Shaw's approaches the round cell type.

All of these are without any alveolar structure and seem to have sprung from the submucosa. Rolleston's case appears to be a large round cell sarcoma without any appearance of alveolation. The origin of his tumor is not clear. Chapman's tumor is difficult to understand; it is alveolated and appears to have sprung from the tissues outside of the œsophagus and to have penetrated its walls. A natural conclusion would be that it arose in a lymph gland, although he describes the cells occupying the alveoli as large, oval and granular.

The tumors may occur at any point in the length of the œsophagus, more frequently they appear in the upper part. They may infiltrate all the coats and project into the lumen of the œsophagus. Necrosis of the superficial parts due to contact with the food masses occurs, and extensive sloughing and ulceration with perforation follow.

Rolleston's and Shaw's cases show wide-spread metastases. The liver has always escaped.

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PAPILLOMA OF THE FALLOPIAN TUBE.

BY J. G. CLARK, M. D.

(*From the Pathological-Anatomical Laboratory of Professor Chiari in Prag.*)

Up to the present time only six cases of simple, non-malignant papilloma of the Fallopian tube have been reported, abstracts of the histories of which, accompanied by a very excellent résumé of the salient points of the subject, have lately been made by Sänger and Barth (Die Krankheiten der Eileiter; Martin, 1895). Of these cases three have been reported by Alban Doran, two by Bland Sutton and one by Doleris.

Doran, who first called attention to the subject, inclined to the theory that these growths are not so much tumors as a simple hyperplastic process produced by chronic inflammation.

On account of the rarity of these cases the following well-marked example, which Prof. Chiari has kindly placed at my disposal for study, appears worthy of report.

HISTORY OF THE CASE.

Museum specimen No. 4769. A cystic tumor removed by Prof. Bayer, from a woman aged 60, June 11, 1892.

The following clinical notes were obtained by Prof. Bayer from Dr. Slansky, the attending physician.

The patient had never miscarried or given birth to a full-term child, and until one year ago had been healthy. At that time she discovered a tumor in the abdomen, which, according to her statement, completely disappeared after a thermal cure, but later again appeared. During the first months of the year 1892 she was confined to bed on three occasions, first for three weeks, then for eight days, and again for three weeks, with attacks of peritonitis. After her recovery she consulted her physician with regard to the abdominal tumor.

Her general condition, as noted at that time by Dr. Slansky, was as follows: A rather weakly built, emaciated woman, of good facial color; heart and lungs normal; tongue slightly coated. The hypogastrium presents the vaulted appearance of a woman six months pregnant. The tumor which gives this appearance to the abdomen is globular, elastic, fluctuating, and in its upper part, towards the groin, is somewhat movable. The cervix is movable, the uterus is deviated to the right, and although the fundus cannot be palpated, it appears to be small and adherent to the tumor, which lies to the right. By digital examination a point in Douglas' cul-de-sac a considerable distance above the cystic tumor may be reached.

From this examination Dr. Slansky diagnosticated an ovarian cyst of the right side and advised its extirpation.

Owing to violent retching by the incompletely narcotized patient, during the preliminary cleansing of the abdomen the cyst was ruptured, and at once became soft and flat, and on physical examination free fluid could be demonstrated in the sides. Upon opening the abdomen, the contents of the cyst, a viscid, clear, honey-yellow fluid, were discharged and the top of the cyst prolapsed through the incision. With this part as a tractor, the entire tumor, which now appeared to be about the size of a child's head, was drawn out upon the abdomen and was found to be connected with the right mesometron by a small band-like pedicle about four fingers in length.

The ovary was situated below this pedicle and appeared perfectly normal. The central part of the pedicle consisted of the uterine half of the right Fallopian tube, which passed over into the tumor, where it became lost. In view of these points the diagnosis of an ovarian cyst was abandoned, and the thought of a parovarian cyst came much more prominently into mind. The pedicle was ligated in several sections and cut through transversely, after which the stump was cauterized, and separate ligatures were applied to all of the larger vessels. The contents of the cyst remaining in the abdomen after extirpation of the tumor were evacuated as completely as possible by rolling the patient over on her side The convalescence was uninterrupted and the patient was discharged well.

MACROSCOPICAL DESCRIPTION.

Cystic tumor half the size of a man's head (12 x 12 cm.), presenting at one spot an amputated surface 4 cm. square, at one point of which is a very short pedicle having the appearance of the enlarged uterine end of the Fallopian tube. Close to the point of amputation is an irregularly torn opening, through which the fluid contents of the cyst have escaped.

The exterior of the tumor is smooth, and in the superficial parts of the wall there are a few large dilated blood-vessels, wandering in irregular tortuous channels, while in the deeper parts an occasional necrotic area is noted.

The internal surface is almost completely covered with a thick papillary growth, consisting of multiple fungus-like excrescences, which, in some areas, are massed together in thick dense clumps, presenting a typical cauliflower appearance. The branches of these excrescences vary in size from delicate fimbriæ to large fusiform projections which contain small cysts. At one place, not far from the point of amputation, are circular folds, some of which reach the height of ½ cm., only covered with delicate velvet-like and small knobbed excrescences. The arrangement and general appearance of these folds at once remind one of those in the normal Fallopian tube. Bordering this area is a palm-sized surface devoid of papillary excrescences.

Upon spreading the excrescences apart, they are found in some parts of the cyst to spring from folds resembling those just described. Here and there these folds have become adherent and pressed back against the cyst wall, forming locculated spaces, some of which also contain papillary growths.

MICROSCOPICAL DESCRIPTION.

Sections through the circular folds show a greatly attenuated cyst wall measuring only 0.05 to 0.1 cm. in thickness. Layers of tissue are seen in the following order, counting from the outside towards the cyst cavity: peritoneum, circular muscle fibers, thin stratum of connective tissue, longitudinal muscle fibers followed by a denser layer of connective tissue, upon which one layer of columnar epithelium arranged in regular order rests. Except in the bay-like projections between the folds, the epithelium is non-ciliated, and even in these spaces the ciliated cells are only rarely found.

Numerous large dilated blood-vessels occupy the connective tissue layer beneath the epithelium. The folds of the Fallopian tube, as such, are no longer present, but are represented by sessile and pedunculated papillary growths.

The low sessile projections are composed of dense connective tissue, like that seen in chronic inflammation of the tube, whose cells extend at right angles from the underlying circular fibers, forming warty prominences clad with one layer of columnar epithelium which gradually shades off into the low columnar and cuboidal variety as the domes of the projections are reached. Besides the sessile excrescences there are a few long, slender processes to which are attached daughter offshoots. The main stem in all instances contains large dilated blood-vessels. The connective tissue forming the stroma of these papillæ shows a marked variation in its structure in different areas. At the bases of the papillæ the cells are closely crowded together and contain deeply-staining spindle-shaped nuclei. This appearance is maintained until the apices or domes of the growths are approached, when the cells gradually become hyaline, and in turn shade off into a pure mucoid degeneration.

Sections from the thicker portions of the cyst wall (0.5 cm. thick) show unstriated muscle fibers scattered very sparsely among the connective tissue fibers which make up the chief part of the section. The internal surface of the cyst wall is covered with innumerable, vigorous growing papillomata, whose main stems extend far out into the lumen of the cyst, forming the most complicated, coral-like systems. The offshoots have, in many instances, coalesced, forming spaces which contain small papillary growths.

In some instances the main stems have become adherent to each other, enclosing much larger gland-like spaces. The mucoid degeneration noted above is even more marked here, and in the large fusiform ends of some of the branches the entire stroma has undergone this transformation, giving the cystic appearance noted in the macroscopical description. Hemorrhage has occurred into some of these spaces containing the mucous tissue, leaving a granular debris which stains a bright yellow by Van Gieson's method.

The ends undergoing degeneration are covered by one layer of shrunken cuboidal epithelium, which rests upon a thin layer of hyaline connective tissue. Besides the cystic spaces formed by the fusion of the papillomata, others are found occupying a deeper portion of the cyst wall, lined by cuboidal epithelium and surrounded by a dense connective tissue stroma like those seen in "sacto-salphinx pseudo-follicularis." (*Martin.*)

In one of these spaces a small papilloma is seen in process of formation. The single layer of cuboidal epithelium lining the

cavity forms an uninterrupted line, except at one point, where it assumes a columnar shape and becomes heaped upon a delicate connective tissue papilla projecting from the main stroma.

CONCLUDING NOTE.

In a general survey of the sections taken from various parts of the cyst wall the muscular tissue appears to be much less abundant and the connective tissue greatly increased over that seen in the normal tube. The papillomatous growths throughout have a non-malignant appearance, the epithelium being in general one-layered and at no place tends to invade the underlying tissue.

According to Sänger and Barth the differential diagnosis in these cases is rendered difficult on account of the tendency of all new growths of the Fallopian tube to assume a papillary appearance; in this case, however, its non-malignant character is so evident that its recognition is comparatively easy.

The early stages of primary carcinoma, before the epithelial cells have deeply penetrated the underlying tissue, or have formed metastatic foci in adjacent parts of the tube, may closely simulate the non-malignant papillary growths, especially where the latter possess the low wart-like form first described by Rokitansky and Hennig.

On account of the marked tendency as pointed out by Williams which papillomata of the ovary show to undergo cancerous degeneration, these growths of the tube must also be looked upon with suspicion, for even if they do not become malignant they may give rise to transplantation growths to the peritoneum, which may so seriously impair the function of this organ as to cause death.

From the foregoing history it appears that the patient suffered with repeated attacks of pelvic inflammation, and the histological examination of the tube shows a condition similar to that seen in chronic inflammation of the tube, plus the papillomatous growths, which sustains throughout the theory advanced by Alban Doran, that papillomata of the tube are but the after-results of inflammatory changes. While some of the smaller growths, especially the sessile ones seen on the remaining folds of the tube, appear as simple hyperplastic processes, as suggested by Doran, the majority are essentially new growths, in which there is a great increase in the connective tissue associated with proliferation of the epithelium.

Bland Sutton has recorded a case similar to the foregoing one, which he classifies as an adenoma, holding to Hennig's original theory that the spaces between the folds of the tube are glands, and therefore new growths which affect them are of the glandular type.

Sänger and Barth quite properly reject Sutton's classification, substituting for it the term *papilloma tubæ cysticum s. vesiculosum*. As our case presents, besides the papillomatous growths, the cystic spaces, it can properly be classified under this title.

THE HISTO-PATHOLOGY OF HERPES IRIS. WITH REPORT OF TWO CASES.

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Although herpes iris as a clinical entity has been recognized since the early part of the century,* and notwithstanding the fact that considerable clinical knowledge has been added by dermatologists during the last few years, comparatively little attention has been directed to its histo-pathology. Even such an extensive writer as Unna has given but a very unsatisfactory description of its pathology, and the usual account which one finds in looking through the literature of the subject may be practically summed up as follows: Oedema, vascular dilatation and "round cell infiltration" (whatever that may mean). In the following case, in connection with which the opportunity of a very complete investigation from clinical, pathological and bacteriological standpoints was offered, many interesting features presented themselves, which seem worthy of some attention and may possibly lead to a clue as to its etiology.

On December 4, 1897, there appeared in the Dispensary of the Johns Hopkins Hospital a case presenting vesiculo-bullous lesions on the skin, concerning which the following history was obtained. The patient was a girl eight years of age, fairly well developed, slight but not thin, with dark hair and complexion. She seemed bright and intelligent, and was in fact somewhat precocious. Her antecedents did not reveal anything of interest.

Family History. Her father, mother and brother are all living and in good health.

History. Personally, beyond one attack of measles which occurred two years ago, and habitual constipation, the patient had always been in good health up to the present time. She had, however, always been, as her mother expressed it, "a nervous child." Her present trouble began two weeks before applying for treatment. At that time she was vaccinated and now has the remains of a fairly typical vesicle on her arm. Directly after the vaccination she began to complain of flushes of heat and chilly sensations, the latter being of a transitory nature. These symptoms were ascribed to the vaccination and no particular attention was paid to them.

In a few days there appeared on the extensor surface of the right forearm "a blister" which was about the size of a split pea when first noticed. This was soon followed by others of like character in the same region, and also upon the left forearm and wrist, together with isolated lesions scattered over the trunk and lower extremities. She was taken to the family physician, who pronounced the case as one of "poisoning"

* Bateman and Willan (1810).

(meaning Rhus toxicodendron), which is quite common in and about Baltimore. A patent mixture of sarsaparilla compound was ordered,* but no local treatment, other than bicarbonate of soda baths, was given.

Present Condition. The patient upon examination presented an eruption, consisting of vesicles and bullæ varying in size from one to five millimeters in diameter, mostly discrete (though some showed signs of confluence), and arising from apparently normal skin. They were tensely filled with a clear colorless fluid, and the lesions which had existed for a day or two possessed a slight erythematous halo, and their contents had become opaque. These lesions occurred principally upon the extensor surfaces of the forearms (Figs. I, II, III), the right being the more affected, though scattered vesicles were found upon other regions, as follows: one small discrete vesicle was to be seen upon the tip of the right ear, a group of similar ones just beneath the chin, and a few discrete lesions on the buttocks. Upon the dorsum of the right foot were also a number of vesicles less developed than those of the regions mentioned. The mucous membranes were free of any eruption, with the exception of a small herpetiform group upon the inner surface of the vulva. The majority of the lesions were discrete and showed but little tendency to group. One bulla upon the right forearm (probably the first to appear) was sunken at the center, its roof having become adherent to the base, and the peripheral portion, still being tense and filled with opaque fluid, presented the appearance of having been formed by the confluence of smaller lesions which had surrounded a central bulla. No marked subjective symptoms were complained of other than the malaise already mentioned, which still persisted, and a slight feeling of tenseness and itching of the cutaneous lesions, which was most troublesome at night. The itching, however, must have been very slight, as neither excoriations nor ruptured bullæ were observed.

At this stage of the eruption erythema bullosum was principally thought of on account of the distribution, but the character of the lesions seemed to point to the pemphigus group, and liquor potassii arsenitis was ordered as an aid to diagnosis. At the same time two vesicles, each of about two millimeters in diameter, situated on the forearm, were excised and dropped into 95 per cent. alcohol for microscopical examination. The patient returned three days later feeling much worse and showing a much more extensive eruption. New vesicular lesions of the character already mentioned had appeared on all the regions previously affected, and the older ones had increased somewhat in size.

The forearms, wrists and backs of the hands and feet were most markedly affected. Upon the back of the right hand was seen a bulla about one-half cm. in diameter surrounded by small (2 mm.) vesicles which had formed a complete circle, the whole patch being situated upon an erythematous base. (See photograph, Fig. I.) Some of the older lesions upon the arms also presented ring-like formations (Fig. II), and the case was now definitely diagnosed as erythema exudativum multiforme, of the bullous variety (herpes iris). Appropriate treatment was ordered and special directions given as regards the diet.

During the next few days no improvement occurred other than the drying up of some of the lesions, which had first appeared and were now desquamating, leaving reddened plaques. New vesicles and bullæ still continued to make their appearance, the duration of each individual lesion being about a week or ten days. No primary lesions other than vesicles and bullæ were noticed. At the end of the first week the patient became confined to her bed, because of the vesicular lesions, which had formed continuous patches on both feet, making walking quite painful.

The temperature at this time was almost constantly above normal (103° being the highest point noted) and slight chills were complained of. The bowels were extremely constipated and the appetite completely lost. The tongue became heavily coated and the breath very foul. During the next few weeks the emaciation became somewhat marked, although the physical examination of the various organs did not reveal anything abnormal. At the end of the second and beginning of the third week the disease was at its height, the patient suffering great discomfort and complaining somewhat of the itching, which seemed to have increased in severity, especially in the lesions on the feet. Pains in the great toe joints were now complained of, the left one being the more affected. This symptom was not constant, as the pain seemed to vary in intensity at different times and was usually worse at night. The lesions now (three weeks after their first appearance) presented all stages of development and resorption and were pretty generally distributed over the entire body.

The regions most affected at this stage were not only the forearms and backs of the hands and legs and dorsal surface of the feet, but the back, thighs, buttocks and perineum also were attacked. Upon the back a large patch 20 cm. in diameter had formed, and the lesions upon the buttocks, perineum and inner surfaces of the thighs were continuous. The neck also was completely encircled by a band of lesions, which extended partly into the hair behind and included both ears.

Smaller, dark venous red colored patches, the ragged edges of which reminded one of the edge of a desquamating syphilitic lesion, and in whose center new vesicles could be seen appearing beneath the thin newly formed epidermis, were situated upon the knees and calves, and about the ankle in the region covered by the shoe. The parts least affected, viz. the upper part of the face, the anterior surface of the thorax, the abdomen, the upper arms, anterior surface of the thighs, and the palms and soles, all showed scattered lesions with large areas of normal skin between them. Even the scalp did not escape entirely, as crusts (probably the remains of aborted vesicles) were noticed in this region, but no true vesicles.

Although comparatively few lesions existed upon the mucous membranes, yet the inner surface of the lips, including the red border, presented fairly numerous aborted vesicles and vesicular detritus; but with these exceptions and one small vesicle upon the hard palate which soon disappeared, no eruption was seen.

During the next three weeks the condition varied, sometimes

* The potassium iodid, which such mixtures usually contain, may have aggravated the eruption; this feature has been noted by many authors, though some report to the contrary.

showing considerable improvement and at others a slight relapse. No return of a temperature above 100° was observed after the time already mentioned. The pains in the joints gradually decreased, both in frequency and severity, and the older lesions began to dry up and desquamate, leaving brownish pigmentations. New vesicles still continued to appear, however, although their number and size were less, and they were mostly discrete and of a shorter duration.

About this time (six weeks after the outbreak) an enlargement of the lymph glands of the right femoral region was noticed. They formed a somewhat tender and doughy mass which measured 3 cm. broad by 6 cm. long. No other glandular enlargements were found. After being eight weeks under treatment the general health of the patient became much improved, in spite of the fact that the parents had insisted on keeping the child at home, where the attentions were of the poorest and the surroundings most squalid. The appetite also returned, and she seemed to be gaining in weight and strength.

Although all the larger patches had now disappeared, leaving pigmented areas, yet there were still quite a number of lesions to be seen, especially upon the backs of the hands and wrists.

Upon the left ankle there was now formed the only lesion other than vesicles or bullæ observed during the entire course, and it also presented the typical iris-like formation. It was composed of four concentric, slightly raised erythematous rings surrounding a darker central spot, and possessed the typical iridescent appearance which characterizes the disease. After twelve weeks had elapsed since the beginning of the attack the child was able to be up and about again; she seemed comparatively well, but came occasionally to the clinic. The hands were still troublesome, and isolated lesions occasionally appeared upon the trunk and extremities, and the attack, therefore, could not yet be said to be at an end. This condition of the skin persisted until about March 30, 1898, when a severe relapse occurred. The photograph shown in Fig. III, was then taken. During this relapse the lesions were almost entirely confined to the forearms and hands. Itching was absent, and among the lesions were many typical of herpes iris. Upon the right arm was to be seen a bulla half surrounded by three semicircular lines of vesicles. A like arrangement occurred upon the left wrist. Remains of other circular patches are also shown in the photograph.

The blood count during this relapse gave the following results regarding the leucocytes:

Polynuclear	70	per cent.
Mononuclear (small),	18	"
" (large),	5	"
Transitional.....	3	"
Eosinophile	8	"

The treatment was symptomatic throughout, and being along well recognized lines laid down by so many dermatologists, need not to be gone into in detail.

During the attack the blood was examined several times, both fresh and in dried and stained specimens.

Erlich's triple stain and eosin and aqueous methyl blue were chiefly used.

Beyond a slight increase of the white-blood corpuscles, observed in the specimens which were taken during the first week, nothing abnormal was noted.

A number of eosinophiles were present in all the preparations, but their relative proportion was, however, not markedly increased. No plasmodia malariæ were found, although their presence was diligently sought for.

The contents of the vesicles were examined fresh and stained *in situ* and after having been mounted, but all gave results which did not differ from the findings in the cutaneous sections which will be described later.

Numerous cultures from the vesicles were made upon slant agar, but no positive results were obtained, with the exception of one tube which showed a growth of the staphylococcus pyogenes albus, probably derived from the surface of the skin.

It may be mentioned here that while dressing the patient, her mother in pressing upon a tense bulla ruptured it suddenly, discharging its contents directly into her eye, from which no results followed.

During the second week of this relapse the patient was admitted into the Johns Hopkins Hospital. During the acute stage the treatment consisted of mild laxatives, strict attention to diet and the application of a mild ointment. Three weeks after the acute stage has passed into a chronic condition Fowler's solution, 2 mins. three times a day was given, and when it was found to be beneficial it was gradually increased to 4 mins. No further relapses occurred but the patient began to improve remarkably in health and all the lesions disappeared. The patient was discharged quite cured four and a half months after the first lesion appeared.

PATHOLOGICAL HISTOLOGY.

The portions of skin taken for examination were from the flexor surface of the forearm, and each represented a vesicle about two millimeters in diameter. They were discrete and arose from apparently normal skin. They were hardened in alcohol and stained with hæmatoxylin and eosin, Loeffleur's blue, Unna's polychrome methylene blue, aniline gentian violet, and by Weigert's method.

The epidermis (Fig. IV) as a whole was practically very little affected, except mechanically. The stratum corneum (*b*) (as one would naturally expect to find it in this region) was of a loose rather than of a compact nature. The stratum lucidum was visible only in places, and was nowhere well defined. The stratum granulosum (*c*) was well marked. It consisted of from one to two layers of cells and was practically unaltered.

The rete mucosum (*d*) showed a slight dilatation of its interepithelial spaces and a consequent increase in depth. This increase, however, was only to be seen at the edges of the vesicle, as over the vesicle itself it was somewhat flattened by the pressure from beneath of the vesicular contents acting against the resistance of the horny layer. The cells of the rete showed no change beyond slight so-called vacuolation, such as is to be observed in many cutaneous affections, as well as in the normal skin. No mitoses were observed above the germinal layers. Here and there, in the inter-epithelial spaces, lymphoid cells and polynuclear leucocytes were found, and near the vesicle a small amount of nuclear detritus. (Fig. IV.)

The corium (Fig. IV, *e*) in the affected area showed acute inflammatory changes, limited to its upper half. These consisted of a localized œdema, marked dilatation of the superficial network of blood-vessels, large numbers of polynuclear leucocytes and a great increase in the number of lymphoid cells. These cells were massed in and about the blood-vessels (*f*), and also scattered about in the connective tissue, making their way toward the epidermis. The papillary body, and more especially the papillæ themselves, were most markedly involved, being the seat of acute œdematous inflammation. The serum appears to have exuded so rapidly that instead of producing a marked œdema of the epidermis, the latter was raised mechanically.

On examining the earliest stage of this pathological condition, which could easily be observed at the periphery of the minute vesicle, one could see how the lesion commenced. In one papilla (Fig. V) the upper third was replaced by serous exudation, as shown by the presence of fine granules and a network of fibrin, among which a number of polynuclear leucocytes were present. These could be seen at all stages of disintegration, from the disappearance of their protoplasm to the breaking up and separation of their nuclei. (Fig. VI.)

The next stage of the process showed the entire papilla filled with coagulated serum, fibrin, and large masses of broken-down nuclei, with only comparatively few polynuclear leucocytes, and the nuclei of a few detached connective tissue cells.

The papillæ in other places were completely destroyed, or flattened out so as to be unrecognizable, their place being taken by a mass of nuclear detritus suspended in a network of fibrin and the remains of the connective tissue. (Fig. VI.)

The vesicle was formed, therefore, by the simultaneous involvement of several neighboring papillæ; the roof being represented by the compressed, but otherwise unaltered epidermis, with the twisted and distorted interpapillary processes dependent from it and extending into the vesicle proper, while the corium with its compressed and swollen papillæ formed the floor.

The contents of the vesicle consisted of a finely granular substance (coagulated serum), strands of fibrin, mononuclear and polynuclear leucocytes, occasional detached epithelial cells, much nuclear detritus and a few eosinophiles.

The lymph vessels were slightly dilated in the vicinity of the vesicle, but the hair follicles, sebaceous glands and sweat coils and ducts were unaffected.

The lower half of the corium showed a slight œdema, but was otherwise normal, as was also the subcutaneous tissue. No micro-organisms were found in sections stained for that purpose.

DIAGNOSIS.

In connection with the diagnosis of this case the chief points to be considered were, (1) its acute onset, (2) the vesicular and bullous character of the lesions, which were frequently to be seen arranged in patches consisting of a contral bulla surrounded by one or more concentric rings of vesicles, as is well depicted in Fig. I, and (3) the symmetrical distribution, which was chiefly upon the forearms and hands, the lower part of the legs and dorsal surface of the feet, appearing first in these regions and persisting there after having disappeared from the other portions of the body.

The marked itching of the lesions on the feet at the height of the attack caused one to think of dermatitis herpetiformis or of pemphigus pruriginosus. According to Duhring, however, the itching in the former disease "is out of all proportion to the eruption," while in the case which has been described it was only when the patient was nearly covered with lesions that this symptom was at all troublesome, and even then it was limited to a portion of the eruption only.

Another point of difference was the purity of the lesional type as already mentioned, in contrast to dermatitis herpetiformis, which even when of the vesicular variety is extremely apt to show a mixture of primary lesions (*i. e.* wheals, vesicles, pustules, etc.) with the vesicular form predominating, while in the present case no lesions other than vesicles and bullæ were noted, with the single exception of a typical patch of iris-like erythematous rings, which tended to strengthen rather than disprove the diagnosis.

From a microscopical standpoint the pictures were about as similar as the clinical, but likewise presented decided differences. Several slides* from a typical case of dermatitis herpetiformis were carefully gone over, the points of difference from the present case being chiefly the enormous number of eosinophiles present in dermatitis herpetiformis and the entire absence of nuclear fragmentation, in contrast to the small number of eosinophiles and the large mass of nuclear fragments present in the sections from the case described.

The blood examinations not showing an increase of the eosinophiles, did not correspond to the reports of Leredde, Perrin and Fordyce, who found an increase of these cells present in the blood of patients with dermatitis herpetiformis.

The diagnosis of pemphigus pruriginosus (a typical case is now under observation at the Johns Hopkins Hospital Dispensary, from which material was obtained for comparison) may be thrown out for similar reasons, as the clinical pictures are seemingly enough different to warrant this. The fact that in pemphigus of this variety there is no tendency to special arrangement of the lesions, and no especial seats of predilection manifested by the eruption, would render such a diagnosis in this case improbable.

CASE II.—In connection with the above case may be mentioned another which appeared a few weeks later. It occurred in a man twenty-six years old, a Russian by birth, and with no regular occupation at the time. His past history was negative, and no reliable data of his family were obtainable.

Three days before applying for treatment he noticed that his hands felt puffy and stiff, and upon compressing the palms he noticed a "blotchy" eruption which had escaped his attention before, being hidden by the natural redness of the skin. Soon after, spots began to appear on the backs of his hands and wrists, and a few also on the feet, which caused enough apprehension to bring him to the Dispensary for treatment.

Upon examination there was found present a slight erup-

* These specimens were from a case already published by Gilchrist (Johns Hopkins Hospital Reports, Vol. I).

tion, limited to the forearms and hands and backs of the feet, which consisted of maculo-papules, roundish in shape, varying from two to three cm. in diameter, and of a dark purplish red color.

Some of these were slightly elevated at the edges, giving them the appearance of having depressed centers. The lesions were discrete and few in number. Upon the palms the above mentioned blotches were to be seen when the skin was compressed so as to cause partial blanching, but were not perceptible otherwise.

Two of the lesions on the forearm showed a tendency to vesiculation, the vesicle appearing as an addition to the maculo-papule. No constitutional symptoms were present, nor were there subjective symptoms of any kind.

Three sections of skin were excised for examination. One represented the macular stage, the lesion selected not being raised above the level of the skin, of a pinkish red color and showing no central depression. The second was a papulo-vesicular formation, the vesicle being about two millimeters in diameter, and situated upon a raised erythematous base which extended about one millimeter beyond it.

At the same time cultures were taken from the other vesicles, which resulted in the growth of staphylococci (pyogenes albus and aureus). The patient was put upon diuretics and laxatives, and all symptoms disappeared in ten days.

The preparations from the excised lesions presented histologically an almost identical picture with those of the first mentioned case, with the following exceptions: The lymph channels of the epidermis were considerably dilated, causing a spreading apart of the epidermal cells, especially of the basal layers, and their consequent detachment upon the formation of the vesicle. This dilatation caused an apparent widening of the entire epidermis, so that over the vesicle it was broader than normal, instead of being compressed.

The destruction of the polynuclear leucocytes, so marked in the first case, was only very slightly present.

The leucocytes were massed at the tips of the papillæ, but appeared in much greater proportion to the amount of serum, the latter having escaped into the epidermis. Otherwise, the findings of the two cases as before mentioned were practically identical in character and correspond in almost every particular with sections prepared from a series of typical cases of erythema exudativum multiforme kindly lent by Dr. Gilchrist for examination and comparison.

Among the various theories of inflammation those formulated by Metchnikoff (although opposed by many eminent pathologists) seem to explain some of the phenomena observed in this case.

According to this author, any foreign substance, upon gaining entrance to the tissues, will (provided it is capable of causing an irritation) exert an attractive power (positive chemotaxis) over the leucocytes.

When the invading body is of a powerful nature as compared with the resisting power of the leucocytes, certain of the latter perish in the attempt to nullify its effects, and are either absorbed by other phagocytes and carried away, or escape as detritus in purulent formations. Whether the substance causing the irritation gains entrance to the tissues from within or without, and whether it is physical, chemical or biological, the result is the same, provided it has or produces other substances which have positive chemotactic properties.

Leloir and Gilchrist have demonstrated in numerous cases of true urticaria that excised urticarial wheals present the picture of an acute inflammation.

Gilchrist has further noticed in factitious wheals, excised from several cases of chronic urticaria (many sections of which were carefully examined) fifteen minutes after irritating the apparently normal skin, that together with the general emigration of leucocytes there occurred a limited destruction of the same, their nuclei appearing as fragments throughout the affected area, this fact suggesting the idea that possibly the mechanical irritation had set free some poison strong enough to attract the leucocytes and to destroy a certain number of them.

Leloir has demonstrated the fact that the lesions of erythema exudativum multiforme show from the beginning the successive steps of an exudative inflammation.

If the cutaneous manifestations of this disease are examined at the earliest stage (at which point many cases cease to develop and the lesions disappear), even at this period a slight migration of the white blood corpuscles may be observed; and as one investigates lesions of a more advanced condition, signs of a more profound disturbance of an inflammatory character are discovered. In herpes iris, representing as it does the most advanced type of erythema exudativum multiforme, the inflammatory process has reached nearly the highest grade shown in primary lesions, the step from the vesicle to the pustule being a slight one.

The observation in Case I of the very rapid breaking down of the polynuclear leucocytes, occurring even as soon as they made their appearance in the papillæ outside of the vessel walls, has not, as far as could be learned, been before reported in connection with this disease, and has suggested the idea that possibly the rapid death was due to a toxine set free from the capillaries of the papillæ, which represent a point of least resistance in the vascular system.

Such a toxine would act as the chemotactic agent, which, in this case, had probably proved powerful enough to cause the death and destruction of the emigrated cells.

What this toxine (if present) is, or how it obtains entrance to the blood stream, is a question which can only be discussed problematically.

The origin of such a toxine might, however, occur in the intestinal canal, and, acting on a nervous system already less resistant than normal, produce the phenomena above described.

The opinion given by some authors, that a toxine causing such a reaction could be formed by some specific micro-organism unrecognizable by present methods of investigation, which gains entrance to the cutaneous tissues through the blood stream, has neither been proved nor disproved as yet.

This hypothesis may seem to combat the term angio-neurosis, and to a certain extent it does, unless the understanding expressed by v. Duhring is accepted. This author says that the term angio-neurosis must be taken "not in an etiological sense . . . but rather as the physiological method by

which the lesions are developed." Schwimmer's definition, that "one designates as vasomotor and angio-neurotic affections all those caused by pathological changes in the innervation of the blood-vessels," is quoted by v. Duhring, who then says, "There is scarcely an hyperæmia, arterial or venous, transient or of long duration, and no inflammation acute or chronic, be what kind it may, that according to this definition one may not designate an angio-neurosis."

Some difference of opinion is to be found in the reports given by the various authors who have written an account of their observation of the histological changes to be seen in herpes iris, especially as regards the formation of the vesicle. Unna, after saying that "the histological examination of the simple erythema multiforme gives almost the same result as that of the vesicular and iris forms," and that "in the latter cases the epidermis changes are more pronounced," and "so far as concerns the changes in the cutis we have . . . altogether four different symptoms: dilatation of the vessels, cell proliferation around the vessel walls, emigration, and œdema of the cutis," goes on to say in reference to the formation of the vesicle, "Where there is actual vesicular development on the border of the eruption we find a marked widening of all the lymph spaces of the epithelium, and in certain spots dilatation into a subcorneal vesicle containing pure lymph. In many eruptions this extends with undermining of the horny layer and neighboring vesicles to a large monolocular blister, under which the prickle layer is simply compressed without undergoing in any sense degenerative changes."

Elliot (Morrow's System of Genito-Urinary and Skin Diseases) says that "vesicles and bullæ are formed by the penetration of the exudation through the intercellular spaces of the rete, and the lifting up of the stratum corneum and portions of the stratum lucidum and granulosum to constitute the outer wall."

Crocker is also of the opinion that the vesicle is formed by the serum "forcing its way between the rete cells."

In contradistinction to these views is that of Gilchrist (Duhring's Cutaneous Medicine), who holds that the vesicle is formed *beneath* the epidermis. It seems not improbable that in cases of the milder form, where the process of vesicular formation is slow and is preceded by the macular or papular forms of erythema, the view of Elliot and Crocker may be correct. With such cases the process observed in Case II might easily be made to conform, with the supposition of a more gradual infiltration of serum. In cases of a more severe type, however, the accumulation of fluid appears to be so rapid that no time is given for the dilatation of the inter-epithelial spaces, and the epithelium is lifted as a whole from the œdematous papillary body, and becomes more or less compressed by the intra-vesicular pressure acting against the resistance of the horny layer.

"Subcorneal vesicles" with the contents of "pure serum," such as Unna describes, were not observed.

The other features in the cases here reported agree in the main with those of other observers. The following exceptions, however, appear. Unna found many mitoses in the perithelia of the blood-vessels and of the epidermal cells. Neither of these locations showed marked proliferation of their respective cells in sections from any of the cases examined, and the point to which special attention has been directed, *i. e.* the fragmentation of the polynuclear leucocytes even immediately after leaving the vessels, does not appear to have been mentioned by any previous observer, and yet it is a fact on which some stress should be laid.

The findings in these two cases are well supported by those of Gilchrist (numerous sections from his six typical cases of the various stages of erythema exudativum multiforme were carefully investigated, the specimens being kindly lent by him for comparison) and it seems probable that the description here given is the correct one as regards the severe type of the exudative erythemata as shown in herpes iris.

RESUMÉ.

The cases here reported represent, in Case I, a severe type of erythema exudativum multiforme bullosum, or herpes iris, which had a protracted course and developed considerable constitutional disturbance.

Case II was of the mild form, the whole attack being limited to two weeks, and only a few of the lesions showing a tendency to vesicular formation.

The distribution and character of the lesions in both cases were typical.

The histopathology may be summarized as an acute exudative inflammation of the upper half of the corium, with dilatation of the superficial network of blood-vessels and lymphatics (the latter being slight), accompanied by a considerable emigration of polynuclear leucocytes, which in Case I became almost immediately disintegrated after leaving the capillaries of the papillæ. The latter, as the process extended, became practically filled with nuclear detritus, and by the confluence of neighboring papillæ similarly affected the vesicle was formed. This phenomenon of nuclear fragmentation does not appear to have been noted by any previous observer.

In Case II, which presented the same general microscopical features, the breaking up of the polynuclear leucocytes was much less marked.

In both cases the vesicle was formed by the lifting of the entire epidermis from the papillary body, the former becoming compressed over the vesicle in Case I, and in Case II appearing swollen and œdematous, and showing more or less dilatation of the inter-epithelial spaces and detachment of the cells of the basal layers of the epithelium. The contents of the vesicles were always the same, and consisted of coagulated serum, polynuclear and mononuclear leucocytes, occasional detached epithelial cells, strands of fibrin, and in Case I much nuclear detritus.

No infarcts of blood-vessels and no hemorrhages were noted.

The sweat apparatus, hair follicles and sebaceous glands were unaffected.

In closing I wish to express my obligations to Dr. T. Caspar Gilchrist of the Johns Hopkins Hospital for his invaluable aid and suggestions in the preparation of this paper.

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Fig. I.

Fig. II.

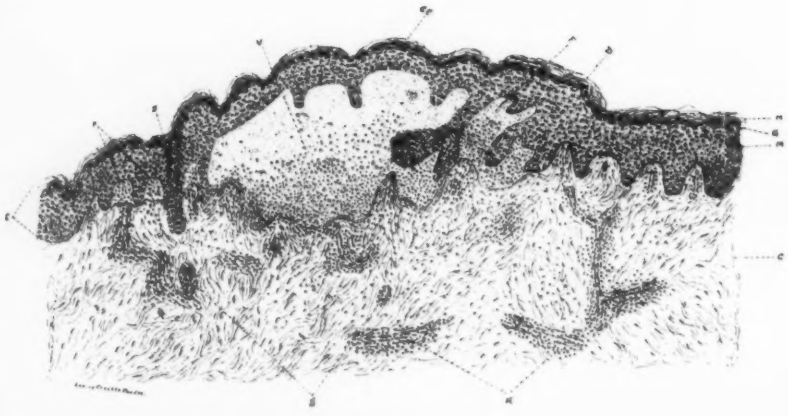

Fig. IV.

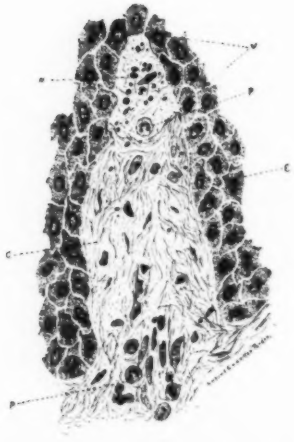

Fig. V.

Fig. III.

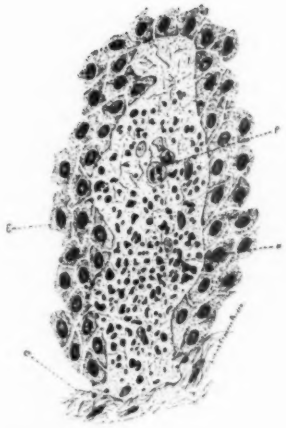

Fig. VI.

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PHOTOGRAPHS OF CASE OF (I) HERPES IRIS.

FIG. I was taken 24 hours after the appearance upon the back of the right hand, of the first lesion characteristic of herpes iris. The central bulla, with a circle of vesicles surrounding it, is well shown. Various sized, tense, discrete vesicles and bullæ, as well as numerous crusts, are scattered over the forearms.

FIG. II represents the antero-external surface of the forearms.

FIG. III shows a relapse 14 weeks after the first attack. The characteristic features of herpes iris are again well developed. In several places four half circles of vesicles have made their appearance.

SECTIONS FROM CASE I.

FIG. IV represents one of the minute vesicles from the forearm. It shows an acute inflammation of the upper half of the corium (*c*). The epidermis (*e*) is practically normal, save a slight increase in depth (*d*) at the edge of the vesicle, and a narrowing over it (*e. e.*). The vesicular formation (*v*) was wholly subepidermal, and its contents were serum, fibrin, mononuclear and polynuclear leucocytes, and much nuclear detritus. (*P*) indicates two papillæ, showing the earliest stage of the process, and (*F*) one somewhat later. (*H*) Horny layer of the epidermis, (*G*) granular and (*M*) prickle layer, (*S*) sweat ducts, (*K*) dilated blood-vessels surrounded by emigrated cells.

FIG. V represents a magnified papilla, with only the two adjoining rows of epidermis (*e*). The earliest stage of the process is shown by the microscopic vesicle (*v*) which has displaced the upper third of the papilla, and contains serum, fibrin, one polynuclear leucocyte (*P*), and fragmented nuclei (*N*). (*C*) connective tissue.

FIG. VI shows a later stage than Fig. V. The entire papilla is here displaced by serum, fibrin, a few polynuclear leucocytes, and a mass of nuclear detritus. Lettering the same as Fig. V.

NOTES ON NEW BOOKS.

The Medical Annual and Practitioner's Index. 1898. Sixteenth year. (*Bristol: John Wright & Co.*)

This volume of the Medical Annual not only will compare favorably with its predecessors, but in some respects it easily exceeds them. The leading articles continue to be supplied by some of the best known writers in the English language and physicians whose interests and field of work especially fit them to present the contributions associated with their names. In a volume containing so much of interest to the busy physician who wishes to be placed *en rapport* with the latest authoritative utterances on medical topics, one can but select a few examples to consider in a brief review. A. Mitra, of Kashmir, supplies the article on bubonic plague. The results of the recent bacteriological and epidemological studies of the outbreaks in China and India are used freely. Attention is called to the contagiousness of the disease, which, it appears, had been rather underestimated. Although the treatment occupies a large part of the article, its richness is embarrassing and depressing rather than inspiring of hope. Thus far no specific remedy has been discovered, and the preventive inoculations of Haffkine and the serum treatment of Borel and Calmette are to be regarded still as *subjudice*. The operation for obliteration of the deformity in Pott's disease, introduced by Calot of Berck-sur-mer, is discussed by Messrs. Jones and Tubby. These writers give an account of the treatment of 56 cases, two of which resulted fatally—"one under circumstances very unsatisfactory," the other from epilepsy five weeks after operation. The tabulated account of these 56 cases will be read with much interest by surgeons. The curves found best suited to treat by this method are (a) those occurring in the young; (b) those in which the disease is active; and (c) those in which the angle of deformity is changing; (d) in those cases where paralysis is present, and as an alternative to laminectomy, which in their experience has often failed to relieve the pressure point. The authors, despite their relatively limited experience which does not permit them to predict unqualified success in this new departure, would yet point out that "the diseased spinal column is no longer too sacred to be touched."

Mr. Shattock has contributed a chapter on the bacteria pathogenic in the human subject, the value of which is greatly enhanced because of the excellent illustrations which accompany it. When this contribution is completed, which it is promised will be achieved in the succeeding volume, the whole will comprise an atlas of pathogenic bacteria very useful to physicians, surgeons and specialists. The drawings are true to nature, and are printed in the colors in which the stained bacteria are usually seen under the microscope. It is a pleasure to recommend this handy volume to the medical profession. S. F.

Jakob: Atlas of Methods of Clinical Investigation, with an Epitome of Clinical Diagnosis, etc. Edited by AUGUSTUS A. ESHNER, M. D. Authorized translation from the German. (*Philadelphia: W. B. Saunders*, 1898.)

A properly executed atlas on clinical diagnosis is to be commended very warmly. Undoubtedly this is the age in medical teaching and practice in which intuition, the so-called "Aerztliches Gefühl," counts for least. Instead of tradition and authority we have substituted observation and experiment and the practitioner who follows in the march of clinical methods resorts to the stethoscope and perhaps the fluoroscope, counts and studies the

blood, estimates the percentage of hæmoglobin, differentiates the several kinds of leucocytes, collects the serum for the Widal test, looks carefully at the urinary sediment, neglects not the diazo-reaction, gives test-breakfasts and analyzes the stomach contents, stains the sputa for bacteria, makes bacteriological cultures from the blood, and at last perchance follows the patient into the dead-house and post-mortem chamber. The small and handy volume under consideration is designed to be an aid to these and many other operations, by supplying as far as possible life-like reproductions of the various appearances observed in health and disease in the blood, urine, stomach and intestinal contents, viscera, etc. The plates in the volume cover the normal histology of the red and white blood corpuscles, the special changes in the blood in leukæmia, pernicious anæmia, leucocytosis, malaria, relapsing fever, anthrax, etc. The blood spectra are given and blood crystals represented. The microscopic appearances of the buccal and nasal secretion in gingival deposit, thrush, diphtheria, etc., and reproductions of unstained and stained (asthma, etc.) sputa in health, cardiac disease, actinomycosis of the lung, etc., are given. Next follow plates representative of the microscopy of the contents of the stomach and intestines, the most important color reactions of the gastric juice, urinary sediments, crystalline and organized, the most important color-reactions of the urine, the commoner pyogenic micro-organisms, etc. Part II is devoted to normal projection of the viscera and percutory topography. The diseases of the lungs, heart and abdominal organs are represented in outline. The concluding part of the volume treats of the various steps embraced in the physical examination, and discusses briefly the special pathology and therapy of the more important diseases.

This very convenient volume can be recommended unhesitatingly to the practising physician no less than to the student in clinical microscopy and physical diagnosis. S. F.

The Elements of Clinical Diagnosis. By Professor G. Klemperer, First American from the seventh German edition. Translated by N. E. Brill, M. D., and S. M. Brickner, M. D., of New York. (*The Macmillan Company*, 1898.)

This work appears to be the result of an attempt to state as much regarding clinical diagnosis in as small space as possible. As a result clearness is apt to be sacrificed to brevity, and accurate description to space. There are many excellent points in the book, but one needs a previous knowledge to appreciate them. A student using it for a text-book frequently would be apt to be led into error, especially through many statements made without necessary qualification. Parts of the book are put clearly and well. Many of the illustrations would have been better left out; they leave much to be desired.

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LOUIS EUGENE LIVINGOOD, M. D.

At a meeting held at noon on the eighth of July, in the office of the Superintendent of the Johns Hopkins Hospital, presided over by Prof. W. H. Welch, the following resolutions were adopted:

Whereas, on the Fourth of July the steamship La Bourgogne sank at sea with more than 500 passengers; and

Whereas, among those lost was our beloved colleague, Louis Eugene Livingood;

Be it Resolved, That we, the Medical Faculty of the Johns Hopkins University and the staff of the Johns Hopkins Hospital, who for five years have been his associates and friends, do express to his family our deepest and most heartfelt sympathy in their cruel bereavement.

He has left a record of unusual purity of character, of singleness of purpose, of devotion to duty, of work well done, which will remain a treasured memory to all who knew him.

And, Be it Further Resolved, That a copy of these resolutions be transmitted to his family and published in the Baltimore News and in the Bulletin of the Johns Hopkins Hospital.

George W. Dobbin,
Lewellys F. Barker,
William Sydney Thayer,
Committee.

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The required period of study for the degree of Doctor of Medicine is four years. The academic year begins on the first of October and ends the middle of June, with short recesses at Christmas and Easter.

Men and women are admitted upon the same terms.

In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

REQUIREMENTS FOR ADMISSION.

As candidates for the degree of Doctor of Medicine the school receives:

1. Those who have satisfactorily completed the Chemical-Biological course which leads to the A. B. degree in this university.

2. Graduates of approved colleges or scientific schools who can furnish evidence: (*a*) That they have acquaintance with Latin and a good reading knowledge of French and German; (*b*) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study.

They are required to furnish certificates from officers of the colleges or scientific schools where they have studied, as to the courses pursued in physics, chemistry, and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school, will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

Hearers and special workers, not candidates for a degree, will be received at the discretion of the Faculty.

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Applicants for admission to advanced standing must furnish evidence (1) that the foregoing terms of admission as regards preliminary training have been fulfilled, (2) that courses equivalent in kind and amount to those given here, preceding that year of the course for admission to which application is made, have been satisfactorily completed, and (3) must pass examinations at the beginning of the session in October in all the subjects that have been already pursued by the class to which admission is sought. Certificates of standing elsewhere cannot be accepted in place of these examinations.

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